CLONIDINE AS AN ADJUVANT TO ROPIVACAINE IN SCIATIC FEMORAL BLOCK FOR LOWER LIMB SURGERY

A STUDY OF 60 CASES

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

BRANCH – X (ANAESTHESIOLOGY)

APRIL-2012

THE TAMILNADU Dr. M.G.R MEDICAL UNIVERSITY

CHENNAI

TAMILNADU

BONAFIDE CERTIFICATE

This to certify that this dissertation entitled **CLONIDINE AS AN ADJUVANT TO ROPIVACAINE IN SCIATIC FEMORAL BLOCK FOR LOWER LIMB SURGERY** is a bonafide record work done by Dr.A.ANBUMURUGARAJ under my direct supervision and guidance, submitted to the Tamilnadu Dr. M.G.R. Medical University in partial fulfilment of university regulation for MD, Branch X – Anaesthesiology

PROF. Dr.T.THIRUNAVUKKARASU, M.D, D.A,

Director, i/c.

Institute Of Anaesthesiology,

Govt. Madurai Medical College & Hospital

Madurai.

DECLARATION

I **Dr. A.ANBUMURUGARAJ** solemnly declare that this dissertation titled **"CLONIDINE AS AN ADJUVANT TO ROPIVACAINE IN SCIATIC FEMORAL BLOCK FOR LOWER LIMB SURGERY"** has been done by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree or diploma to any other University or board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of Doctor of Medicine degree Branch –X (Anaesthesiology) to be held in April 2012.

Place: Madurai **Dr. A.ANBUMURUGARAJ**

Date:

ACKNOWLEDGEMENT

I am deeply indebted to Professor **Dr. T. THIRUNAVUKKARASU, M.D., D.A.,** Director, i/c. Institute of anaesthesiology, Madurai Medical College, Madurai for the able guidance, inspiration and encouragement he rendered at every stage of this study.

I express my heartfelt gratitude to Professor **Dr. S.C. GANESH PRABU M.D., D.A.,** for his able guidance in doing this project.

My sincere thanks to Professor **Dr. R. SHANMUGAM, M.D., D.Ch., &** Professor **Dr. A. PARAMASIVAN M.D, DA.,** for their constant support and their able assistance in completing this study.

I express my profound thanks to assistant professor **Dr.D.S.SUDHAKAR, M.D., DNB.** for his valuable assistance and technical guidance in doing this study.

I am also thankful to my other assistant professors and my post graduate colleagues of Institute of anaesthesiology for their kind co-operation in doing this study

My profound thanks to **Dr. EDVIN JOE, M.D., Dean,** Madurai Medical College and Government Rajaji Hospital, Madurai for permitting to utilize the clinical materials of this hospital in the completion of my dissertation.

Last, but not the least. I gratefully acknowledge my patients who gave their consent and co-operation for this study.

CONTENTS

INTRODUCTION

“For all the happiness that mankind can gain

it is not in pleasure but in relief from pain”

- JOHN DYRDEN

Pain is a fundamental biological phenomenon. The international association for the study of pain has defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage”. Pain is always underestimated and under treated. The relief of pain during surgery is the main part of anaesthesia.

In 1784 James Moore used mechanistic concepts to promote neural compression as a useful technique for the provision of surgical anaesthesia.

In 1855, it was proposed that neurologic pain can be treated by circum-neural injection of pain relieving drug. At the same year Gadecke (Germany) isolated alkaloid from leaves of coca plant. In 1860 Albert Nieemann was successful in isolating and naming the alkaloid from the leaves of erythroxylon coca.

In 1880 Halsted and Hall began their work on regional anaesthesia. In 1884 Hall reported that injection of cocaine into the forearm provided analgesia below the point of injection. Additional blocks were then

performed on the brachial plexus, infraorbital nerve and sciatic nerve, all for operative surgery.

After introduction of barbiturate and cyclopropane, the enthusiasm for block anaesthesia waned in early 1940s. In current recent years however, the technique has had resurgence, due in large part to increased understanding of neural plasticity and the possibility of minimizing hospital stay length by effective use of regional block anaesthesia.

Several techniques have been used to prolong the duration of regional anaesthesia. The continuous infusion of local anaesthetics through catheters in nerve blocks are extensively studied and recently opioids as adjuvants to local anaesthetic solutions were used.

Surgery in the leg results in severe and sustained postoperative pain. This postoperative pain is difficult to control with oral medications. Single shot nerve block is very effective for postoperative pain control in orthopaedic and surgical procedures.

Sciatic nerve has a wide sensory distribution, hence it can be used together with saphenous or femoral nerve block for any surgical procedures below the knee. This form of anaesthesia avoids sympathectomy associated with neuraxial blocks and may therefore be advantageous when any shift in hemodynamics could be deleterious.

Several experimental and clinical studies have shown that Alpha - 2 adrenergic agonists like clonidine were able to prolong sensory and motor blockade.

This study is designed to assess the efficacy of the addition of an alpha -2 adrenergic agonist, Clonidine to local analgesic solution in sciatic femoral block for lower limb surgery.

AIM OF THE STUDY

To assess the efficacy of **CLONIDINE AS AN ADJUVANT TO ROPIVACAINE IN SCIATIC FEMORAL NERVE BLOCK** in respect to

1. Onset and duration of sensory blockade
2. Onset and duration of motor blockade
3. Duration of postoperative analgesia
4. Haemodynamic changes
5. Sedation score and
6. Side effects

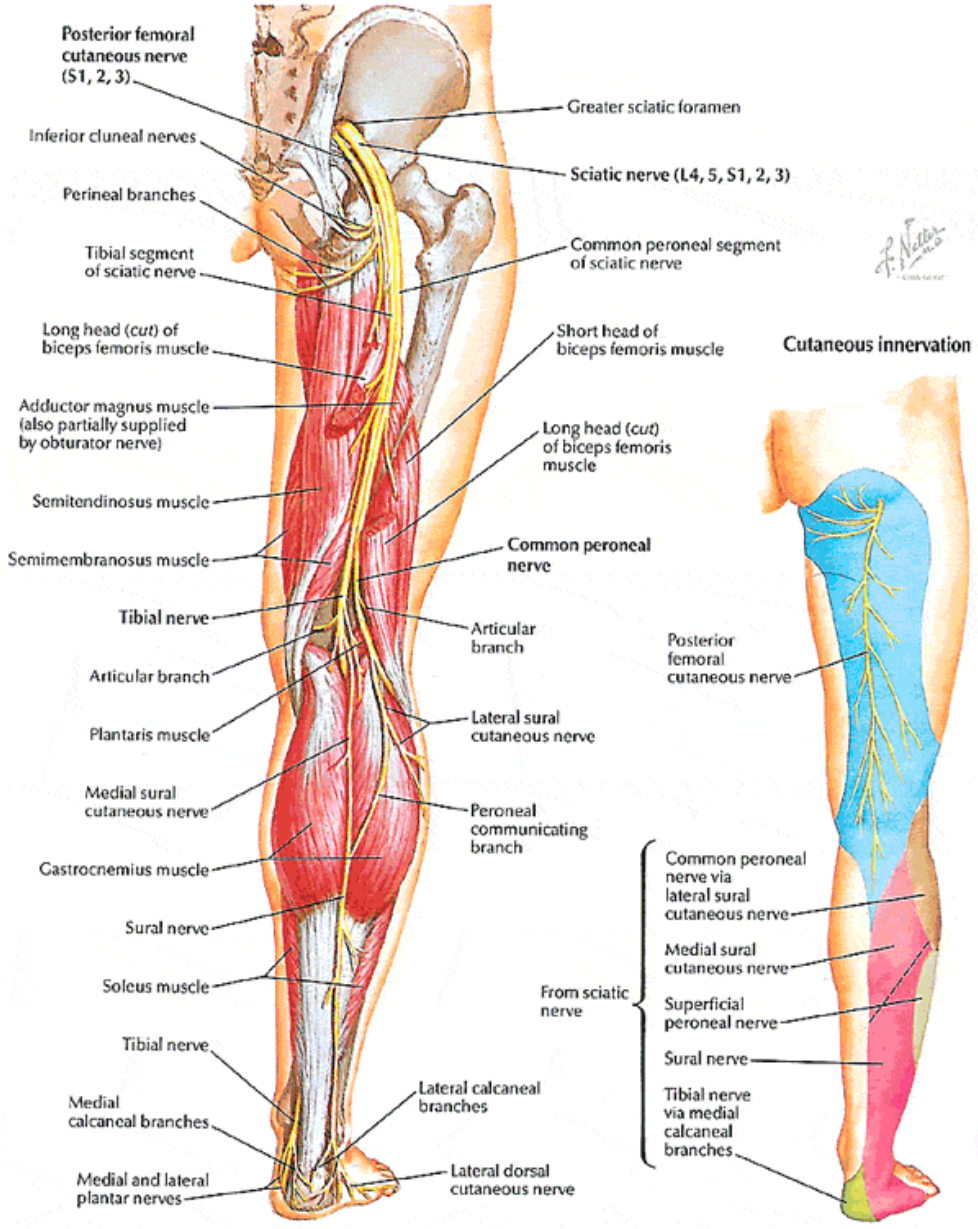
ANATOMICAL CONSIDERATIONS

Knowledge of the formation of sciatic and femoral nerve and of its distribution is absolutely essential to the intelligent and effective use of sciatic femoral nerve block. As the sciatic nerve is deeply situated within the muscular plane, there are various approaches to sciatic nerve blockade.

FORMATION OF SCIATIC NERVE:

The largest of the four major nerves supplying the leg is the sciatic nerve (L4-L5, S1-S3). The sciatic nerve arises from the sacral plexus, where it is nearly 2 cm in width as it leaves the pelvis in company with posterior cutaneous nerve of the thigh. It passes from the pelvis through sacrosciatic foramen beneath the lower margin of pyriformis muscle and between the tuberosity of the ischium and greater trochanter of the femur. The nerve becomes superficial at the lower border of the gluteus maximus muscle. From there it courses down the posterior aspect of the thigh to the popliteal fossa, where it divides into tibial and common peroneal nerves. Branches supplying the posterior thigh are given off during the descent of the nerve to the popliteal space. The sciatic nerve supplies sensory innervations to the posterior thigh and entire leg and foot from just below the knee

DISTRIBUTION OF SCIATIC NERVE



Tibial nerve:

The tibial part of the sciatic nerve, either before or after its separation from the common peroneal nerve, supplies branches to all muscles in the posterior compartment of thigh (long head of biceps femoris, semimembranosus, semitendinosus) except the short head of biceps femoris, which is innervated by the common fibular part. The tibial nerve descends through the popliteal fossa, enters the posterior compartment of leg and continues into the sole of the foot.

The tibial nerve innervates:

1. All muscles in the posterior compartment of leg.
2. All intrinsic muscles in the sole of the foot except the first two dorsal interossei muscles, which are innervated by the deep fibular nerve.
3. Skin on the posterolateral side of the lower half of the leg and medial side of the ankle, foot, and little toe, and skin on the sole of the foot and toes.

Common peroneal nerve :

The common peroneal part of the sciatic nerve innervates the short head of biceps femoris in the posterior compartment of thigh and then continues into the lateral and anterior compartments of leg and onto the foot

The common peroneal nerve innervates:

1. All muscles in the anterior and lateral compartments of leg.
2. One muscle (extensor digitorum brevis) on the dorsal aspect of the foot.
3. The first two dorsal interossei muscles in the sole of the foot.
4. Skin over the lateral aspect of the leg, and ankle, and over the dorsal aspect of the foot and toes.

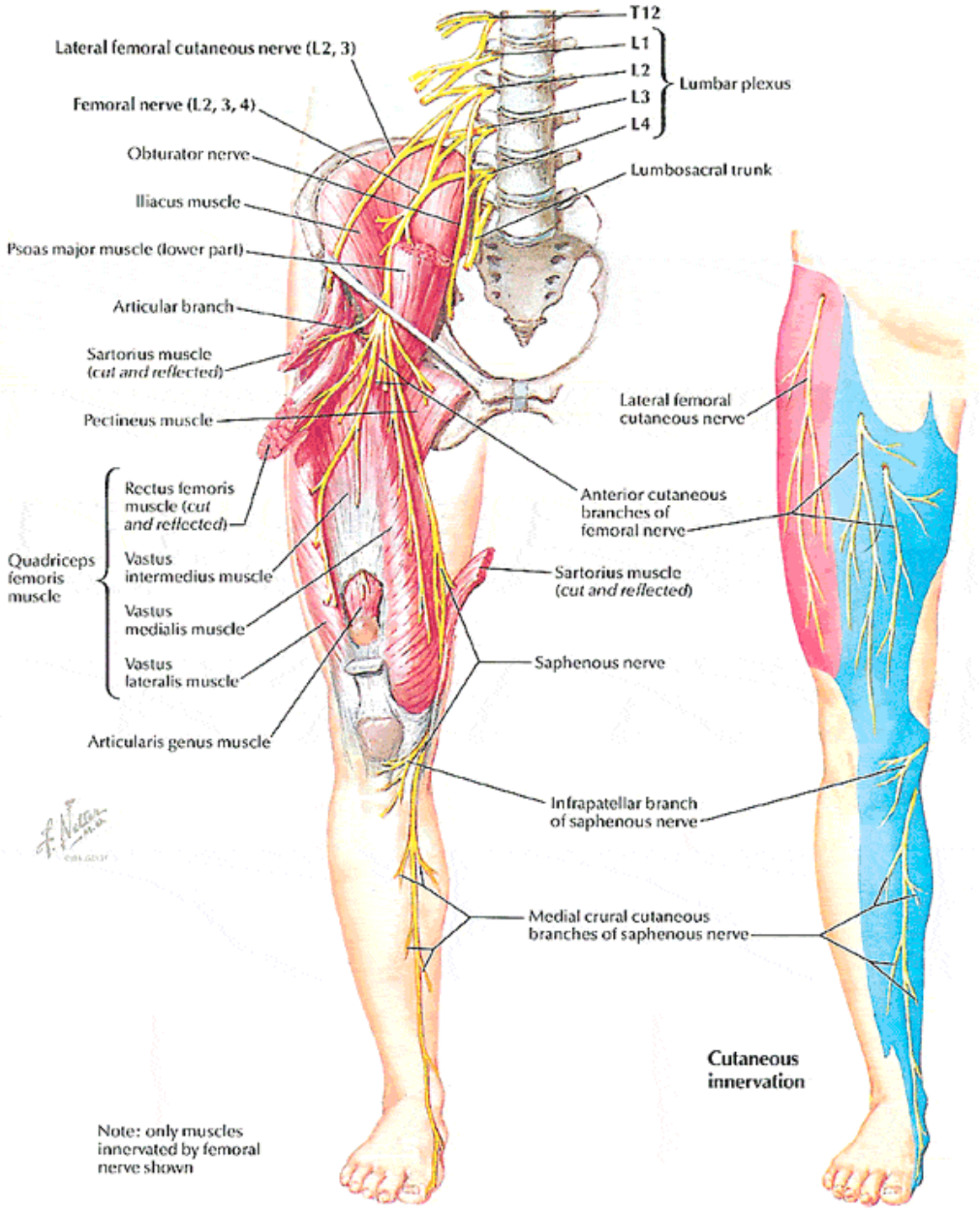
FEMORAL NERVE:

The femoral nerve (L2-L4) proceeds from the lumbar plexus in the groove between psoas major and iliac muscles, where it enters the thigh by passing deep to the inguinal ligament. At the level of inguinal ligament, the femoral nerve lies anterior to iliopsoas muscle and slightly lateral to the femoral artery. Immediately after passing under the inguinal ligament, the femoral nerve divides into anterior and posterior divisions.

Branches of the femoral nerve include:

1. Anterior cutaneous branches, which penetrate deep fascia to supply skin on the front of the thigh and knee.
2. Numerous motor nerves, which supply the quadriceps femoris muscles (rectus femoris, vastus lateralis, vastus intermedius, and vastus medialis muscles) and the sartorius muscle.
3. One long cutaneous nerve, the saphenous nerve, which supplies skin as far distally as the medial side of the foot.

DISTRIBUTION OF FEMORAL NERVE



TECHNIQUE OF BLOCKADE:

SCIATIC NERVE BLOCK – POSTERIOR APPROACH

ANATOMICAL LANDMARKS:

Important bony structures for posterior sciatic nerve block include greater trochanter of femur, posterior superior iliac spine and sacral hiatus. The greater trochanter can be identified by palpating the lateral aspect of proximal femur, walking upwards, one finger tends to fall off the bone when the apex of greater trochanter is reached. The posterior superior iliac spine is the bony prominence at the posterior end of iliac crest. Palpation from the iliac crest can help to correctly identify the posterior superior iliac supine.

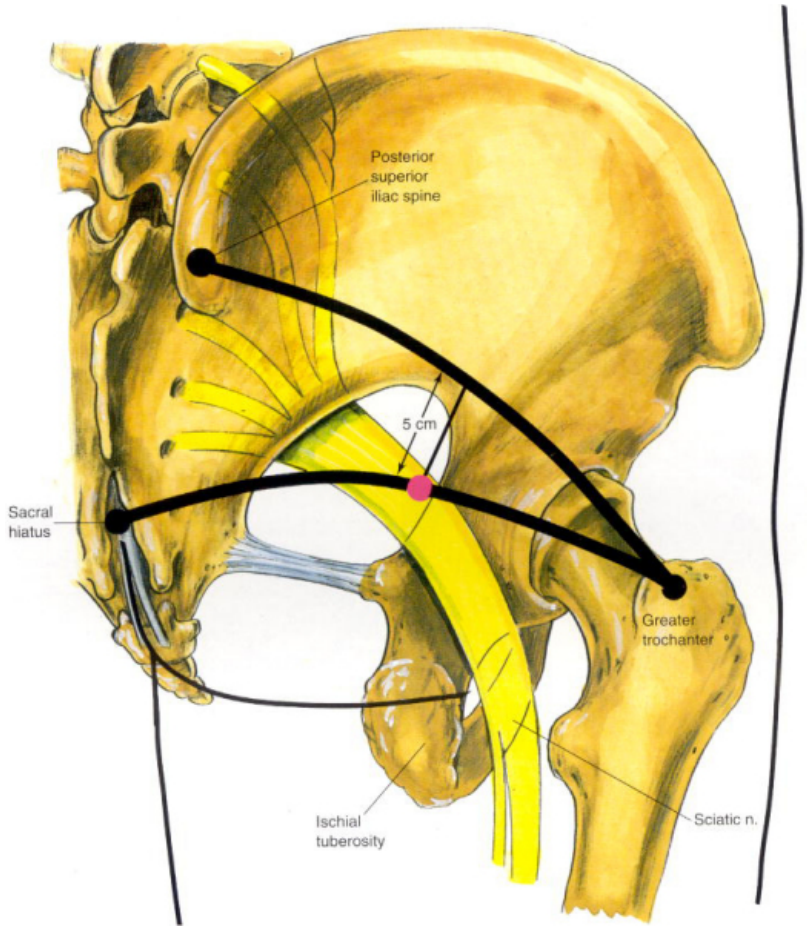
POSITION OF THE PATIENT:

The posterior approach to the sciatic nerve block is with the patient lying on the side opposite the one to be blocked rolled forward onto the flexed knee, with the heel in opposition to the knee of the outstretched dependent leg.

TECHNIQUE:

The patient is placed in lateral (sims) position. The first line is drawn between points made over the upper aspect of greater trochanter of the femur and posterior superior iliac spine. This line is bisected and a perpendicular line is drawn passing downwards from its midpoint. A second line is drawn from the sacral hiatus to the greater trochanter. The point at which this line

ANATOMICAL LANDMARKS – SCIATIC NERVE



intersects with the perpendicular line marks the point of insertion. The area is prepared and draped. A skin wheal performed with 1ml of lignocaine (1%) using a hypodermic needle at the point of insertion. A 21 gauge short-beveled and 50mm long Teflon-coated needle is connected to the peripheral nerve stimulator which is set at 1 mA with 2 Hz frequency. The needle is inserted perpendicular to both sides and oriented 90 degrees to all the planes and varied slowly until muscle twitching of the leg and foot is observed. The stimulation is gradually reduced to lower than 0.5mA while muscle twitching is observed. The volume of local anaesthetics (0.75% ropivacaine) is 18 ml.

COMPLICATIONS:

1. Neural injury is rare with the use of nerve stimulator, but still possible.
2. Local anaesthetic toxicity due to intravascular injection. Hence slow injection and carefull aspiration should be done before giving the drug.
3. Haematoma due to puncture of inferior gluteal vessels.

Other approaches to sciatic nerve blockade are anterior or beck approach, inferior approach, subgluteal approach and lateral approach.

FEMORAL NERVE BLOCK:

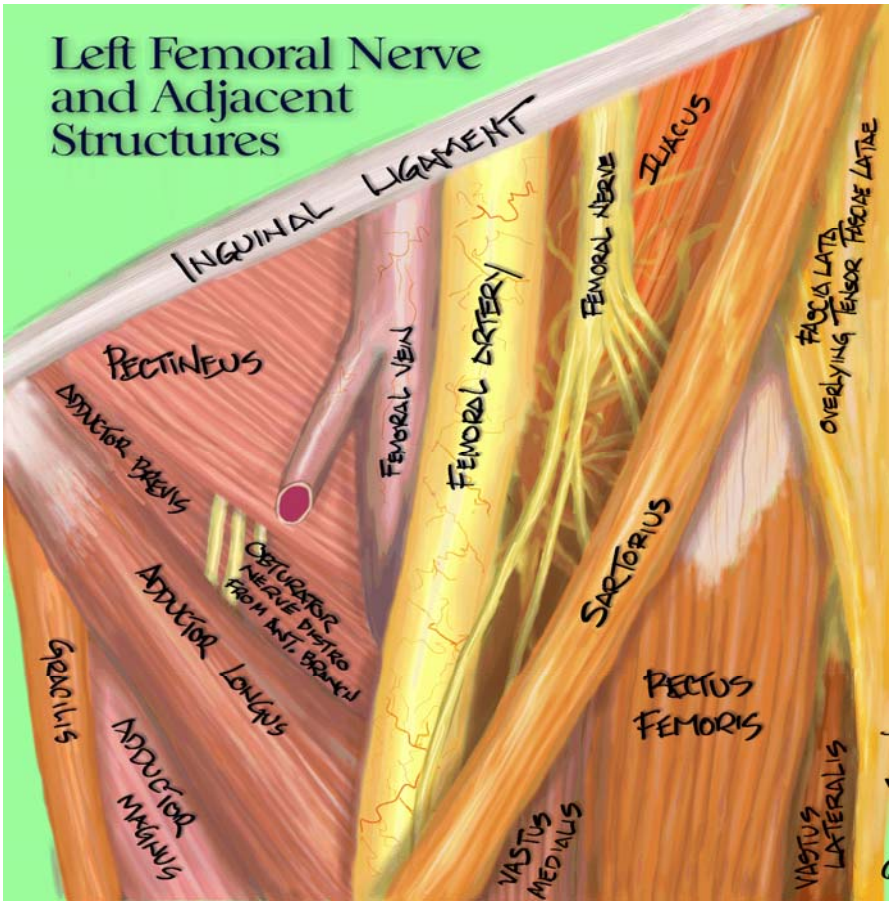
ANATOMICAL LANDMARKS

The main landmarks for femoral block are the anterior superior iliac spine, the pubic tubercle, inguinal ligament, inguinal crease and femoral artery.

TECHNIQUE:

The patient is placed in supine position. The pubic tubercle can be palpated three finger breadth from the midline, along the upper border of the pubis. The inguinal ligament is outlined by a line connecting the anterior superior iliac spine and pubic tubercle. The femoral artery lies approximately at the intersection of the medial third and lateral two thirds of the inguinal ligament (mid inguinal point). The femoral nerve which is found lateral to femoral artery is noted and marked as insertion point. The area is prepared and draped. A skin wheal performed with 1ml of lignocaine (1%) using a 23g hypodermic needle at the point of insertion. A 23 gauge short-beveled and 50mm long Teflon-coated needle is connected to the peripheral nerve stimulator which is set at 1 mA with 2 Hz frequency. The needle inserted and oriented in a 45 degree cephalad and advanced slowly until the appropriate muscle response is observed-quadriceps contraction with resultant rhythmic patellar movement. The

ANATOMICAL LANDMARKS – FEMORAL NERVE



needle position is adjusted while decreasing the current to 0.5 mA with the maintenance of muscle response. The volume of local anaesthetics (0.75% ropivacaine) is 12 ml.

PHYSIOLOGICAL CONSIDERATIONS

Pain perception requires noxious stimuli. It is transformed from its native form by the activated nociceptors into electrical signals which are then transmitted along the corresponding nociceptive fibres. These fibres in turn synapse onto second order neurons in the spinal cord. These interneurons are located in the dorsal horn. It is at these interneurons where the initial modulation of nociceptive input occurs. From the spinal cord nociceptive input is transmitted to the brain stem, thalamus and cortex.

Peripheral neuroanatomy of nociception

C and A delta fibres are the main peripheral nociceptors. The skin, joints and periosteum are richly innervated with C and A delta nociceptors.

A delta fibres are responsible for the sensation of first pain (the initial sharp pain experienced following an injury). C fibres are unmyelinated and are responsible for second pain (the slowly building throbbing burning pain experienced following an injury).

CLASSIFICATION OF SENSORY FIBRES

Sensory receptors	Speed of transmission	Sensory function	Myelination
C Fibres	0.5 -2m/sec	Noxious chemical, Mechanical, thermal activation (Slow burning second pain)	Unmyelinated
A-Alpha fibres	70 -120m/sec	Noxious chemical thermal, mechanical stimuli, (sharp fast, first pain)	Lightly myelinated
A-Beta fibres	30 -70m/sec	Non painful, light, touch, pressure, vibration proprioception	Heavily myelinated
A-Gamma fibres	30-70m/sec	Proprioception/Motor to muscle spindle	Myelinated
A-Delta fibres	12 -30 m/sec	Pain, cold, touch	Myelinated
B fibres	3 -15 m/sec	Preganglionic autonomic (sympathetic)	Myelinated

Peripheral neurochemistry and neurotransmitters

Commonly released inflammatory mediators implicated in pain and hyperalgesia include bradykinins, potassium, substance P, cytokines, histamine, serotonin and prostaglandins.These peripheral neurotransmitters either activate or sensitise the peripheral nociceptors to pain.

PERIPHERAL NEURO CHEMISTRY ALGOGENIC AGENTS

Algogenic Agent	Action on nociceptors
Bradykinin	Activates
Potassium	Activates
Substance P	Sensitizes
Arachidonic acid	Sensitizes
Cytokiness	Sensitizes
Serotonin	Sensitizes
Nor adrenaline	High concentration activates and sensitizes after injury.

Peripheral alpha 2 receptors

Alpha 2 adrenoreceptors are located on primary afferent terminals, on neurons in the superficial laminae of the spinal cord, and within several brainstem nuclei implicated in analgesia, supporting the possibility of analgesic action at peripheral, spinal, and brainstem sites.

Clonidine enhances both sensory and motor blockade from peripheral nerve injection and epidural/spinal injection of local anaesthetics. Clonidine blocks conduction of C and A gamma fibers and increase potassium conductance in isolated neurons and intensifies

conduction block of local anaesthetics. Local vasoconstriction resulting in reduced absorption from injection site was another point of discussion, but compared with adrenaline as adjuvant it failed to influence plasma levels, indicating a direct action on nerve.

PAIN PATHWAY:

SPINAL CORD

The gray matter of the spinal cord is divided into ten lamina with lamina I – IV representing the dorsal horn. The dorsal horn is capped by the Lissauer's tract which consists of branches of cutaneous A and C fibres and few visceral afferents.

Nociceptive fibres terminate in the superficial layers of lamina I & II while the non-painful myelinated fibres terminate in the deeper layers of lamina III, IV. Lamina II has the highest concentration of opioid receptors in the spinal cord. Modulation and inhibition of nociception may occur at this level through the use of opioids (systemic and neuraxial).

ASCENDING SENSORY PATHWAYS

Peripheral sensory neurons synapse onto the secondary interneurons of the dorsal horn. The axons of the non nocieptive secondary neurons travel ipsilaterally in the dorsal columns of the spinal cord as **fasciculus**

cuneatus (upper body through T6) and **fasciculus gracilis** (lower body below T6) and synapse in thalamus.

The axons of the nociceptive secondary neurons after synapsing, travel contralaterally in the anterolateral aspects of the spinal cord as the neospinothalamic and paleospinothalamic tract.

Neospinothalamic tract carries fine discrimination of pain eg. Location, intensity and first pain.

Paleospinothalamic tract responds to noxious stimuli. The paleo spinothalamic tract synapses in the thalamus, hypothalamus and limbic system and plays a role in emotional aspects of pain via limbic system. The thalamus has multiple connections to limbic system and cortex.

DESCENDING INHIBITORY PATHWAYS

The descending controls of pain project specifically onto laminas I,II,V of the dorsal horn from mesencephalon, raphenuclei and reticular tract. The mesencephalon is rich in opioid receptors. This area sends excitatory transmissions to the rostroventral medulla which sends nordrenaline and serotonin to inhibitory tracts via the dorsolateral funiculus to lamina I, II, V of spinal cord.

The noradrenaline and serotonin fibres mediate transmission between the primary afferents and the secondary neurons of the dorsal

horn. Increased activity of these fibres leads to increased inhibition of pain transmission.

Location of Alpha2 receptors

Primary afferent terminals, on neurons in the superficial laminae of spinal cord and brainstem nuclei.

Location of opioid receptors (central)

Opioid receptors are found in the various regions in CNS namely, cerebral cortex, limbic cortex (anterior and posterior amygdala, hippocampus, hypothalamus, medial thalamus, mid brain, periaqueductal gray matter, extrapyramidal areas, substantia gelatinosa and sympathetic preganglionic neurons.

Opioid receptors are also found in the cardiac sympathetic fibres, cardiac branches of vagus, adrenal medulla and gastro intestinal tract.

NERVE STIMULATOR

History:

The first description of electrical stimulation to locate the brachial plexus was recorded by Perthes in 1912. However, the acceptance of peripheral nerve blocks was not realized until the 1960s when electronic advances and the consequent introduction of more convenient solid-state units were made. Greenblatt and Denson have demonstrated that motor nerves can be stimulated without eliciting pain and that the current required to stimulate the nerve depends on the distance between the needle and the target nerve.

The mapper–locator is an excellent solution to reduce the dependency of the anaesthesiologist on anatomical knowledge and variations, and also increases the success rate compared to the paraesthesia technique. It is helpful in defining anatomical land marks for the entry point, especially in growing children ,obese patients and in case of distorted anatomy.

Components:

The nerve stimulator case contains an on/off switch and a dial, selecting the amplitude of the current. It has two leads to complete the circuit. One lead is connected to an ECG skin electrode and the other lead

to the locating needle. The polarity of the leads should be clearly indicated and colour-coded with the negative lead being attached to the needle.

Mechnism of action:

A small current (0.25-0.5mA) is used to stimulate the nerve fibres causing the motor fibre to contract. The frequency is set at 1-2Hz. The duration of the stimulus should be short (1-2ms) to generate painless motor contraction.

The nerve stimulator is battery operated to improve patient safety. Nerve location can be very accurately defined especially when low currents are used. The success rate of technically difficult nerve blocks can be increased by using a nerve stimulator. A sciatic nerve block with a success rate of over 90% can be achieved in experienced hands, compared to about 50% without using a nerve stimulator.

Nerve blocks can be performed while the patient is anaesthetized or heavily sedated as the response is visibly monitored with no need to elicit paraesthesia. However, the use of neuromuscular blocking agents will abolish any muscular contractions

Problems in practice and safety features:

Higher currents will stimulate nerve fibres even if the tip of the needle is not adjacent to the nerve. The muscle fibres themselves can also

be directly stimulated when a high current is used. In both situations the outcome will be an unsuccessful block once the local anaesthetic solution has been injected.

It is not recommended to use nerve stimulator designed to monitor the extent of neuromuscular blockade for regional nerve blocks. These are high output devices which can damage the nervous tissue.

PHARMACOLOGY OF ROPIVACAINE

Ropivacaine is a new aminoamide local anaesthetic. It is the monohydrate of the hydrochloride salt of 1–propyl–2pipecoloxylidide. Pipecoloxylidides were first synthesized in 1957 and have been in clinical use of more than 30 years. Ropivacaine has a propyl group on the piperidine nitrogen atom of the molecule.

The Pipecoloxylidides are chiral drugs because the molecules possess an asymmetric carbon atom and they may have left – (sinister) or right (rectus) handed configuration.

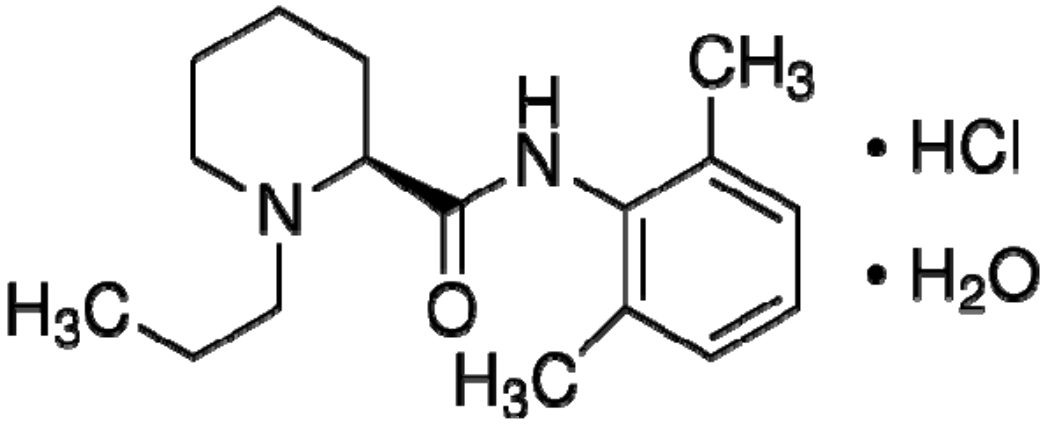
Ropivacaine hydrochloride is an odourless, clear liquid and is manufactured in the pure S-enatiomer form by the alkylation of S–enantiomer of dibenzoy–L –tartaric acid. It has an enantiomeric purity of 99.5%.

PHYSIO-CHEMICAL PROPERTIES

The physio-chemical properties of Ropivacaine are as follows:

1. Molecular weight (base) - 274
2. pKa - 8.1
3. Partition Coefficient (N Heptane buffer) - 2.9
4. Mean uptake ratio TMsense nerve - 94

ROPIVACAINE HYDROCHLORIDE



PHARMACOLOGIC PROPERTIES

The relative lipid solubility of ropivacaine as measured by partitioning studies between N-heptane buffer and relative mean uptake into rat sciatic nerves, shows ropivacaine to be intermediate between bupivacaine and lignocaine. Plasma – protein binding is marginally less than of bupivacaine but the pKa is identical. It has a moderate onset,long duration of action with relative potency of 6.

MECHANISM OF ACTION

Ropivacaine acts by reversible blockade of the sodium ion channel found in the nerve cell membranes. The decreased permeability of the membrane to sodium ions produce a decrease in depolarisation velocity and an increase in excitable threshold, temporarily preventing the transmission of nerve impulses. The progression of anaesthesia is related to the diameter, myelination and conduction velocity of affected nerve fibers.

The order of loss of nerve function clinically is as follows**:**

1. Pain
2. Temperature
3. Touch
4. Proprioception

5. Skeletal muscle tone.

PHARMACOKINETICS

In human volunteers the pharmacokinetic characteristics of ropivacaine have been determined after intravenous infusion

Clearance	0.82 ± 0.16 litres /min
Plasma protein binding	94 %
Volume of distribution at steady state	59 ± 7 liters
Terminal elimination ½ life	111 ± 62min

Metabolism in liver is by aromatic hydroxylation by cytochrome P_{450} 1A to 3 – hydroxyl ropivacaine.

Excretion-86% via the kidney 1%-unchanged drug, rest as metabolites. The higher clearance of ropivacaine over bupivacaine is advantageous in terms of lesser systemic toxicity.

ABSORPTION

The systemic concentration of ropivacaine is dependent on the total dose and concentration of drug administered, the route of administration, the patient's haemodynamic condition and the vascularity of the administration site. From the epidural space, ropivacaine shows complete and biphasic absorption. The slow absorption is the rate limiting factor in

the elimination of ropivacaine, which is why the terminal half life is longer after epidural than after intravenous administration.

DISTRIBUTION

After intravascular infusion, ropivacaine has a steady state volume of distribution of 59 ±7 litres. Ropivacaine is 94% protein bound, mainly to $\alpha_1$acid glycoprotein. An increase in total plasma concentration during continuous epidural infusion has been observed, related to postoperative increase of $\alpha_1$acid glycoprotein. Variation in unbound, i.e. pharmacologically active concentrations have been less than in total plasma concentrations. Ropivacaine readily crosses the placenta and rapidly equilibrium is reached in regard to unbound concentration.

METABOLISM

Ropivacaine is extensively metabolized in the liver, mainly by aromatic hydroxylation mediated by cytochrome P450 1A with 86% of a single dose being metabolized and only 1% being excreted unchanged in urine. The major metabolites are 3–hydroxy ropivacaine 2,6 pipecoloxylidide (2.8%) and 4-hydroxy ropivacaine(0.4%). Small quatities of 3- hydroxyl pipecoloxylidide and 2-hydroxy methyl ropivacaine are also formed. Cytochrome P1A2 is the major enzyme system responsible for formation of 3-hydroxy ropivacaine while cytochrome 3A4 is

responsible for the formation of 2,6 pipecoloxylidide. Because of the dependence on the cytochrome system for metabolism, there is a potential for the metabolism of ropivacaine to be inhibited by competitive drugs such theophylline and imipramine. The quinolones, fluoxamine and verapamil are potent inhibitors of cytochromeP1A2 and could reduce the metabolism of ropivacaine. In animal studies 3- hydroxyl and 4- hydroxyl ropivacaine have been shown to have a weak local anesthetic activity but this is not proven in clinical use. There is no evidence that ropivacaine undergoes racemisation during metabolism or elimination.

ELIMINATION

The kidney is the main excretory organ for most local anaesthetic metabolites. In total 86% of the ropivacaine dose is excreted in the urine after intravenous administration of which only 1% relates to unchanged drug. Ropivacaine has a mean total plasma clearance of 387 ±107 ml/min. The mean ± SD terminal half life is 1.8 ± 0.7 h after intravascular administration and 4.2 ± 1.0 h after epidural administration.

PHARMOCODYNAMICS

Primary Pharmocodynamics (Animal Studies)

These studies showed that ropivacaine at low concentration produced a profound rapid block of both A delta and C fibres and was more potent than similar low concentrations of bupivacaine.

At higher concentrations, ropivacaine and bupivacaine had similar blocking properties. A delta fibre blocking was 16% greater than bupivacaine and the degree of C fibre block was similar with both the drugs.

Ropivacaine is a potent producer of frequency (or use) dependant blocks (i.e) a block that occurs only when the fibre is stimulated. Ropivacaine blocked 'C' fibres faster than A fibres.

Low pKa and high lipid solubility of a local anaesthetic drug favoured A over C fibre block. The lower lipid solubility of ropivacaine over bupivacaine is presumed to retard penetration into myelin sheath.

This greater degree of differential block with ropivacaine at low concentration and the property of producing frequency dependent block were considered to offer clinical advantages in providing analgesia with minimal motor block.

Secondary Pharmocodynamics:

Addition of epinephrine to ropivacaine has no limiting effect on the systemic absorption of ropivacaine. Systemic absorption can produce effects on the central nervous and cardiovascular systems. At blood concentration achieved with therapeutic doses, changes in cardiac conduction, excitability, refractoriness, contractility and peripheral vascular resistance are minimal. However, toxic blood concentrations depress cardiac conduction and excitability, which may lead to atrioventricular block, ventricular arrhythmias and to cardiac arrest. In addition, myocardial contractility is depressed and peripheral vasodilatation occurs, leading to decreased cardiac output and arterial blood pressure.

Ropivacaine can produce central nervous system stimulation, depression or both. Apparent central stimulation is usually manifested as restlessness, tremors, shivering, progressing to convulsions, followed by depression and coma, progressing to respiratory arrest. However, ropivacaine has a primary depressant effect on the medulla .

ADVERSE REACTIONS

A major cause of adverse reactions may be due to excessive plasma levels that may be due to over dosage, unintentional intravascular injection

or slow metabolic degradation. Most adverse events reported were mild and transient.

CENTRAL NERVOUS SYSTEM REACTIONS

These are characterized by excitation and/or depression. Restlessness, anxiety, dizziness, tinnitus, blurred vision or tremors may occur, possibly proceeding to convulsions. However, excitement may be transient or absent with depression being the first manifestation. This may quickly be followed by drowsiness, unconsciousness and respiratory arrest. Other effects may be nausea, vomiting, chills and constriction of pupils.

CARDIOVASCULAR SYSTEM REACTIONS

High doses or unintentional intravascular injection may lead to high plasma levels and related depression of myocardium, decreased cardiac output, heart block, hypotension, bradycardia and ventricular arrhythmias including ventricular tachycardia and ventricular fibrillation and possibly cardiac arrest.

Preparations available:

0.2%

0.5%

0.75%

1%.

Uses:

1. Infiltration anaesthesia
2. Peripheral nerve blocks
3. Lumbar extradural block (Especially Labour)
4. Subarachnoid block
5. Caudal block

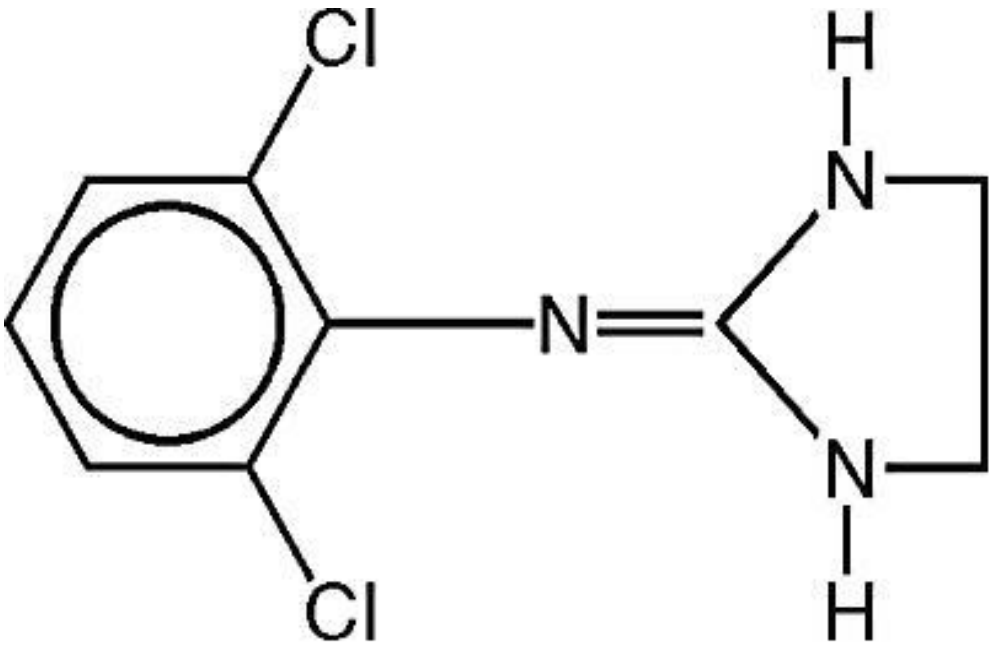
PHARMACOLOGY OF CLONIDINE

Clonidine hydrochloride is a centrally acting selective partial α2 agonist introduced in early 1960s, it was during its use as a nasal decongestant that its anti–hypertensive property was found out. Subsequently more insights into the pharmacological properties has led to its use in clinical anaesthesia practice as well.

Clonidine hydrochloride is an imidazoline derivative and exists as a mesomeric compound. The chemical name is 2-(2,6 dichlorophenylamino) -2 imidazoline hydrochloride. The structural formula is C9H9Cl2N3HCl.

The molecular weight is 266.56. Clonidine hydrochloride is a white crystalline odourless powder with a bitter taste. It is produced by chemical synthesis and it is soluble in alcohol and water. Clonidine improves the quality of anaesthesia, provides a more stable cardiovascular course during anaesthesia, and reduces the dose requirement of the anaesthetic agent. Clonidine potentiates the anaesthetic action of the local anaesthetics with fewer side effects in peripheral nerve blocks and central neuraxial blockade.

CLONIDINE HYDROCHLORIDE



AVAILABILITY

Available as one ml ampoule containing 150 micrograms. It should be stored below 25 degree celsius. It is also available in tablet, containing 100 micrograms.

MECHANISM OF ACTION

Clonidine is a centrally acting partial α2 adrenergic agonist with a selectivity ration of 220: 1 in favour of α2 receptors. The three subtypes of α2 receptors are α2a, α2b, α2c. α2a receptors mediate sedation, analgesia, sympatholysis. α2b receptors mediate vasoconstriction and anti- shivering. The startle response may reflect the activation of α2c receptors. The drug is lipid soluble, penetrates the blood brain barrier to reach the hypothalamus and medulla when injected epidurally. It stimulates the inhibitory α2 adrenoreceptors to reduce the central neural transmission in the spinal neurons Inhibition of substance-P release is believed to be involved in the analgesic effect.

The α2 adrenoreceptors are located on the afferent terminals of both peripheral and spinal neurons in the superficial laminae of the spinal cord and with in several brain stem nuclei implicated in analgesia. The superficial laminae contain three groups of neurons: tonic, adapting, single- spike firing, all of which receive their primary sensory input from

Aδ and C fibres. Clonidine inhibits voltage gated Na + and K+ channels and suppresses the generation of action potentials in tonic- firing spinal dorsal horn neurons, contributing to analgesic effect. The ability of clonidine to modify the function of potassium channels in the CNS (Cell membrane become hyperpolarized) may be the mechanism for profound decrease in anaesthetic requirements.

Another contribution to analgesic effect may be through the release of acetylcholine in the neuraxial region. The α2 adrenergic agonists also enhance analgesia from intraspinal opioids. Sedation is produced by its action on locus ceruleus.

Clonidine affects the blood pressure in a complex fashion after neuraxial or systemic administration because of opposing action at multiple sites. In the nucleus tractus solitarius and locus ceruleus of the brain stem, activation of post-synaptic α2 adrenoreceptors reduces sympathetic drive. It also activates nor- adrenergic imidazoline preferring binding sites in the lateral reticular nucleus producing hypotension and anti- arrythmogenic ation. In the periphery it acts on pre-synaptic α2 adrenoreceptors at sympathetic terminals to reduce the release of nor-epinephrine causing vasorelaxation and reduced chronotropic drive. The brainstem and the peripheral effects of α2 adrenoreceptor stimulation

are counterbalanced by the direct peripheral vasoconstriction through its action on α2 adrenoreceptors from the circulating concentrations of clonidine.

Sedation is a desired property. Clonidine produces a dose dependent sedation at the dose of 50 micrograms or more in less than 20 minutes regardless of the route of administration.

In peripheral nerves it produces a minor degree of blockade at high concentrations with some preference for C- fibres and this effect may, in part enhance the peripheral nerve block when added to local anaesthetics, probably because the α2 adrenoreceptors are lacking on the axons of peripheral nerves.

PHARMACOKINETICS

Clonidine is well absorbed orally and is nearly 100% bio available and reaches peak plasma concentration within 60 to 90 minutes. The mean half life of the drug in plasma is about 9 to 12 hours, with approximately 50% metabolized in the liver where as is it is excreted in an unchanged form by the kidney, and its half- life can dramatically increase in the presence of impaired renal function.

Clonidine is highly lipid soluble and readily distributes into extravascular sites including the central nervous system.

300 micrograms intravenously over 10 min produces:

Distribution t½	:	11± 9 minutes
Elimination t½	:	9± 2 hours
Volume of distribution	:	2.1± 0.4 l/kg
Plasma protein binding	:	20 - 40% in vitro

METABOLISM

Clonidine is approximately 40% cleared by metabolism, predominantly in the liver to five inactive metabolites. The predominant pathways are hydroxylation of the phenyl ring and opening of the imidazoline ring following an initial reductive step with subsequent oxidative cleavage The major metabolite is P-hydroxyclonidine. The hydroxylated metabolites are subjected to secondary conjugation with sulphate or glucuronide prior to urinary excretion.

EXCRETION

70% of the dose, mainly in the form of unchanged parent drug is excreted (40 – 60%) in urine. So, the elimination t ½ of clonidine varies as a function of creatinine clearance.

DOSAGE

Oral	-	3-5µg/kg
Intramuscular	-	2 µg/kg

Intravenous	-	1-3µg/kg
Spinal	-	50 -100µg
Epidural	-	1-2µg/kg
Transdermal	-	0.1-0.3 mg released per day

PRECAUTIONS

1. In patients with renal insufficiency, lower dose is needed.
2. Sudden withdrawal of prolonged continuous epidural infusion produces hypertensive crisis. So it should be gradually discontinued over 2 to 4 days.
3. Use with caution in patients with cerebrovascular or coronary insufficiency.

CONTRAINDICATIONS

1. Known hypersensitivity to clonidine or components of the product.
2. In patients with bradyarrhythmia or AV block.
3. Patients with severe cardiovascular disease.
4. Patients with cardiovascular / hemodynamic instability.

INTERACTIONS

1. Clonidine may potentiate the CNS - depressive effect of alcohol, barbiturates or other sedative drugs.
2. Narcotics may potentiate the hypotensive effects of clonidine.

3. Tricyclic anti depressants may antagonize the hypotensive effects of clonidine.
4. Concomitant administration of drugs with a negative chronotropic, dromotropic effect (beta blocker, digoxin) can cause or potentiate bradycardiac rhythm disturbances.

USES

1. Pre anaesthetic medication :

   Oral clonidine preanaesthetic medication (5μg/kg)

   (a) Blunts reflex tachycardia associated with direct laryngoscopy for intubation of trachea, (b) decrease intraoperative lability of blood pressure and heart rate, (c) decrease plasma catecholamine concentrations, and (d) dramatically decrease anaesthetic requirements for inhaled and injected drugs. Clonidine also attenuates the rise in intraocular pressure associated with laryngoscopy and intubation.
2. Epidural block : Clonidine as sole agent or in combination with opioids or local anaesthetics to provide excellent analgesia in labour pain. Epidural clonidine is also indicated for the treatment of intractable pain, which is unresponsive to maximum does of oral opioid, as do patients with reflex sympathetic dystrophy and neuropathic pain.

3. Spinal anaesthesia: Clonidine combined with local anaesthetics improves the quality and duration of the block, minimize the tourniquet pain during lower limb surgery, and prevents shivering.
4. Caudal anaesthesia: Clonidine combined with local anaesthetics increases the duration of anaesthesia and analgesia by 2 or 3 times without hemodynamic side effects.
5. Peripheral nerve blocks: Clonidine prolongs the duration of anaesthesia and analgesia with local anaesthetics by two times in a dose of 75 to 150 micro grams.
6. Bier's Block: 150 microgram of clonidine enhances the tolerance of tourniquet.
7. It is also used in intra articular analgesia.
8. Protection against perioperative myocardial ischemia; clonidine decreases myocardial ischemia, infarction and mortality following cardiovascular surgery.
9. To treat hypertensive crises.
10. Diagnosis of pheochromocytoma; 0.3 mg will decrease the plasma concentrations of catecholamine in normal patients but not in the presence of pheochromocytoma.

11. Treatment of shivering : Administration of clonidine,75µg IV stops shivering by inhibiting thermoregulatory control.
12. Treatment of opioid and alcohol withdrawl syndrome.

SIDE EFFECTS

1. The most common side effects are sedation and xerostomia.
2. Cardiovascular complaints are bradycardia, hypotension, and ECG abnormalities like junctional bradycardia, high degree AV block and arrhythmia are reported rarely. Occasionally requires treatment of bradycardia with I.V anticholinergics. Orthostatic hypotension occurs rarely.
3. Rebound hypertension; Abrupt discontinuation of clonidine can result in rebound hypertension as soon as 8 hours and as late as 36 hours after the last dose. Symptoms of nervousness, diaphoresis, headache, abdominal pain, and tachycardia often precede the actual increase in systemic blood pressure. Labetalol is useful in treatment of rebound hypertension.
4. Skin rashes occurs rarely.

OVER DOSAGE

There is no specific antidote for clonidine overdosage. Supportive measures like atropine, ephedrine, and i.v. fluids are required for treatment.

Yohimbine an alpha blocker partially reverses the analgesia and sedation but not the heart rate and blood pressure.

REVIEW OF LITERATURE

1. Andrea casati et al, ANAESTHESIA ANALGESIA 2000, concluded small dose clonidine prolonged postoperative analgesia after sciatic femoral nerve block with ropivacaine. In this study 30 patients were randomly allocated in two groups, in which group A, 15 patients received 30 ml of 0.75% ropivacaine and in group B, 15 patients received 30 ml of 0.75% ropivacaine and 1µg/kg clonidine. There is no significant difference in the onset of sensory and motor blockade in both the groups. Duration of motor block was prolonged in ropivacaine - clonidine group. The mean time from block placement to first request for pain medication was shorter in ropivacaine (13.7 hrs) group when compared to ropivacaine - clonidine group (15.4 hrs). They concluded that 1µg/kg clonidine to 0.75% ropivacaine provided a 3 hour delay in first request of pain medication after hallux valgus repair with no clinically relevant side effects.
2. Guido fanelli et al, ANAESTHESIA ANALGESIA 1998, A double blind comparison of ropivacaine, bupivacaine, and mepivacaine during sciatic and femoral nerve blockade. This study concluded that, for sciatic femoral block, 0.75% ropivacaine has an onset similar to that of

2% mepivacaine and the duration of postoperative analgesia between that of 0.5% bupivacaine and 2% mepivacaine.

3. Eledjam jj, Deschodt j et al, Canadian journal of anaesthesia1991; Brachial plexus block with bupivacaine; effects of added alpha-adrenergic agonists: comparison between clonidine and epinephrine. In this study, 60 patients were randomly allocated in two groups, so that 30 patients were randomly allocated in two groups. So that 30 patients received 150 micrograms of clonidine and 30 patients received 200 micrograms of adrenaline. In clonidine group there is no difference in the onset of sensory blockade and motor blockade when compared to adrenaline group. Duration of motor blockade was prolonged in clonidine group (580.4 ± 38.7vs 290.6 ± 34.5 minutes) when compared to adrenaline group. The block produced with addition of clonidine was longer. (994.2 ± 34.2 Vs 728.3±3 5.8 minutes) and superior to that with adrenaline. The injection of clonidine into the brachial plexus sheath is an attractive alternative to epinephrine to prolong the duration of analgesia following upper limb surgery under conduction anaesthesia.
4. Wolfgang Erlacher et al, Canadian Journal of anaesthesia 2001; Clonidine as an adjuvant for mepivacaine, ropivacaine and bupivacaine in axillary, perivascular brachial plexus block. The study shows that the

addition of clonidine has a different impact on each of the three local anesthetics investigated in terms of onset and duration of block. Mepivacaine group has rapid onset compared to ropivacaine and bupivacaine group. The duration of motor block in the mepivacaine - clonidine group was 468 ± 62 mins vs mepivacaine group was 212± 47 mins, The duration of motor block in ropivacaine- clonidine group was 712 ± 82 mins vs ropivacaine group was 702 ±52 mins. The duration of motor block in bupivacaine-clonidine group was 972± 72 mins vs bupivacaine group was 728± 36mins.

5. Brian M. Ilfeld et al, Anaesthesia Analgesia 2003; Continuous infraclavicular perineural infusion with clonidine and ropivacaine compared with ropivacaine alone. A randomized, double blinded, controlled Study. This study reported that clonidine is often added to long acting local anesthetic perineural infusions in an effort to improve post operative analgesia.
6. Popping DM, Elian et al, Anaesthesiology 2009; clonidine as an adjuvant to local anaestheics for peripheral nerve and plexus block: Meta analysis of randomized trials. This study reported that the clonidine prolonged the duration of post operative analgesia by 122

minutes, sensory blockade by 74 minutes, and motor blockade by 41 minutes.

7. A.casati et al, sciatic nerve block with 0.5% levobupivacaine, 0.75% levobupivacaune and 0.75% ropivacaine: a double- blind randomized comparison. This study concluded that, 0.75% levobupivacaine provides a shorter onset time than 0.5% levobupivacaine and a longer duration of postoperative analgesia than both 0.5% levobupivacaine and 0.75% ropivacaine with reduced need for rescue analgesia after surgery.
8. Gianluca Cappelleri et al, ANAEATHESIA ANALGESIA 2000, Evaluated the effect of the injection technique on the onset time and efficacy of femoral nerve block performed with 0.75% ropivacaine. A total of 30 patients undergoing arthroscopic knee surgery randomly allocated to receive femoral nerve block with 0.75% ropivacaine by using either a single injection or multiple injection. They concluded the study, that searching for multiple muscular twitches shortened the onset time and improved the quality of femoral block with small volumes of 0.75% ropivacaine.
9. Pia di Benedetto et al, ANAESTHESIA ANALGESIA 2002, Compared the posterior popliteal and subgluteal continous sciatic nerve block for anaesthesia and acute postoperative pain management after foot surgery

60 patients were randomly assigned to either a subgluteal or popliteal group. Sciatic nerve block was performed with 20ml of 0.75% ropivacaine using either subgluteal or posterior popliteal approach and the placement of catheter afterwards. The catheter was connected to patient controlled analgesia pump to infuse 0.2% ropivacaine. They concluded that the subgluteal approach is as effective and safe as posterior popliteal approach for continous sciatic block and can be considered a useful alternative to anaesthesia and postoperative analgesia.

10. Fanelli G et al ANAESTHESIOLOGY 1999, Studied the intraoperative and postoperative clinical properties of sciatic - femoral nerve block with either ropivacaine at different concentrations and with mepivacaine. Adult patients scheduled for foot and ankle surgery were randomized to receive combined sciatic-femoral block with 225 mg of either 0.5%,0.75% or 1% ropivacaine and 500mg of 2% mepivacaine. Onset time, adequacy of surgical anaesthesia, time to offset of nerve block and time until first postoperative requirement for pain were evaluated. The study concluded that 0.75% ropivacaine is the most suitable choice of local anaesthetic for combined sciatic- femoral nerve

block, providing an onset similar to mepivacaine and prolonged postoperative analgesia.

11. Pia di Benedetto et al, ANAESTHESIA ANALGESIA 2001, evaluated the efficacy and acceptance of a new posterior subgluteal approach to the sciatic nerve with the classic posterior approach. 128 patients undergoing foot orthopedic procedures were randomly allocated to receive either the classic posterior sciatic nerve block or a modified subgluteus posterior approach. In both groups, a proper sciatic stimulation was elicited at 0.5 mA, then 20 mL of 0.75% ropivacaine was injected. They concluded that this new subgluteal posterior approach to the sciatic nerve is an easy and reliable technique and can be considered an effective alternative to the more traditional Labat's approach.

12. Jacques E. Chelly et al, ANAESTHESIOLOGY 1999, Performed a new anterior approach to sciatic nerve block. Sciatic nerve blocks were performed in 22 patients. A line was drawn between the inferior border of the anterosuperior iliac spine and the superior angle of the pubic symphysis. Next, a perpendicular line bisecting the initial line was drawn and extended 8 cm caudal. The needle was inserted perpendicularly to the skin, and the sciatic nerve was identified at a

depth of 10.5 cm (9.5–13.5 cm; median and range) using a nerve stimulator and a 15-cm beveled insulated needle. After appropriate localization, either 30 ml mepivacaine, 1.5% or 15 ml mepivacaine, 1.5%, plus 15 ml ropivacaine, 0.75%, injected. They concluded that this approach represents an easy and reliable anterior technique for performing sciatic nerve blocks.

13. Pierre Beaulieu et al, ANAESTHESIA ANALGESIA 2006, compared the pharmacodynamics of equal concentrations of bupivacaine and ropivacaine in combined sciatic and femoral nerve blocks for patients undergoing knee arthroplasty. Fifty patients received 40 mL of either 0.5% bupivacaine or 0.5% ropivacaine, before induction of anesthesia. Loss and recovery of sensory and motor functions were recorded in the distribution of the femoral, saphenous, common peroneal, and tibial nerves. Pain scores and morphine consumption over 48 hours were also evaluated. They concluded that block resolution is different between bupivacaine and ropivacaine when administered for combined sciatic and femoral nerve blocks.

14. Casati a, Magistris.L, et al, Minerva Anestesiol 2001, adding clonidine to ropivacaine for axillary approach of brachial plexus block provided prolonged analgesia without side effects of sedation and

cardiovascular homeostasis. In this study 30 patients were allocated to two groups for axillary approach of brachial plexus block. Group I received 20 ml of 0.75% ropivacaine and 1 μg/kg clonidine block. Group II received 20ml of 0.75% ropivacaine alone. Axillary block was performed with nerve locator. There was no difference in demography, degree of sedation, peripheral oxygen saturation and hemodynamic variables observed between the two groups. Readiness of surgery required 5-36 minutes with ropivacaine and 5-30 minutes in ropivacaine-clonidine mixture. The first postoperative analgesic request occurred after 13.8 hours in ropivacaine- clonidine group.

MATERIALS AND METHODS

This study was conducted at Government Rajaji Hospital attached to Madurai medical college. The inclusion criteria being 60 patients of ASA grade I or II of either sex and age more than 20 years undergoing lower limb surgery (mostly orthopedic, vascular and general surgeries).

Patients with allergy to local anaesthetics, peripheral nerve injury, bleeding diathesis, local sepsis, patient refusal, contraindications to clonidine and patients in whom the block was unsuccessful due to total failure of missed dermatomes which needed intravenous supplementation of opioids or general anaesthesia were excluded from the study.

It was a double blinded study in which patients were randomly allocated into two groups, Group R-ropivacaine and Group RC–ropivacaine clonidine. Each group comprises of 30 patients, surgery was done under sciatic femoral nerve block. Preoperative investigations done were haemoglobin, blood sugar, urea, serum creatinine and urine albumin and sugar.

PROCEDURE

After ethical committee approval, informed consent was obtained from the patients. No premedication was given to the patients. Intravenous access was obtained, Anaesthesia machine checked, resuscitative

equipments and drugs were kept ready. Sciatic femoral block was performed by posterior Labats approach after confirmation with nerve stimulator.

In GROUP R: Patients received 30 ml of 0.75% ropivacaine with 0.4 ml normal saline. In this mixture 18 ml is given in sciatic nerve block and 12 ml in femoral nerve block.

In GROUP RC: Patients received 30 ml of 0.75% ropivacaine with 0.4 ml clonidine (60 microgram). In this mixture 18 ml is given in sciatic nerve block and 12 ml in femoral nerve block.

Care was taken so that the toxic doses of the local anaesthetics were not exceeded according to the weight of the patients.

PARAMETERS OBSERVED

1. Onset of analgesia

   Onset of analgesia was taken as abolishment of pin prick pain over the distribution of tibial and femoral nerve and was assessed every minute after the performance of the block.

2. Onset of motor blockade :

   Onset of motor blockade was assessed every 3 minute after the block using four point scales

0 – Normal power

1- Weakness but able to move leg

2- Not able to move leg but able to move the toes

3- Complete motor blockade

Attaining a score of 2 was considered as the onset of motor Block

3. Duration of surgery:

4. Duration of motor Blockade:

When (3) in the four point scale changes to (2) the motor blockade is said to reverse. The duration of motor block is noted from the time from scale (3) to scale (0)

5. Duration of analgesia:

The pain was assessed using visual analogue scale having 10 cm length numbered from 0 to 10. Patient was explained about the visual analogue scale as 0 – No pain and 10 the worst possible pain and was asked the score in visual analogue scale.

The patients was observed every 30 minutes after the surgery was over till the motor block reverses and thereafter hourly for 6 hrs and 2 hourly for next 10 hrs.

a. Duration of absolute pain free period: the post operative period during which the patient did not have pain (VAS -0).

b. Time at which VAS score is greater than 5 was noted and patient was given rescue analgesia as intramuscular NSAID (Injection – Diclofenac).

c. Duration of post operative analgesia; the period of time after the surgery till the patient needs analgesic (VAS score more than 5).

6. Vital parameters:

   Pulse rate,

   Blood pressure,

   SPO2.

7. Ramsay sedation score:

   1. Awake & alert
   2. Sedated, responding to verbal commands
   3. Responding to physical stimulus
   4. Responding to moderate & severe physical stimulus
   5. Not arousable

8. Side effects noted are

   Hypotension

   Bradycardia

DATA ANALYSIS

The information collected regarding all the selected cases were recorded in a master chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2010)** developed by centre for disease control, Atlanta.

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

STATISTICAL ANALYSIS

This study comprised of two groups. The patients in group R received ropivacaine 0.75% 30ml + 0.4ml normal saline. In group RC received 0.75% ropivacaine 30ml + 60 microgram of clonidine.

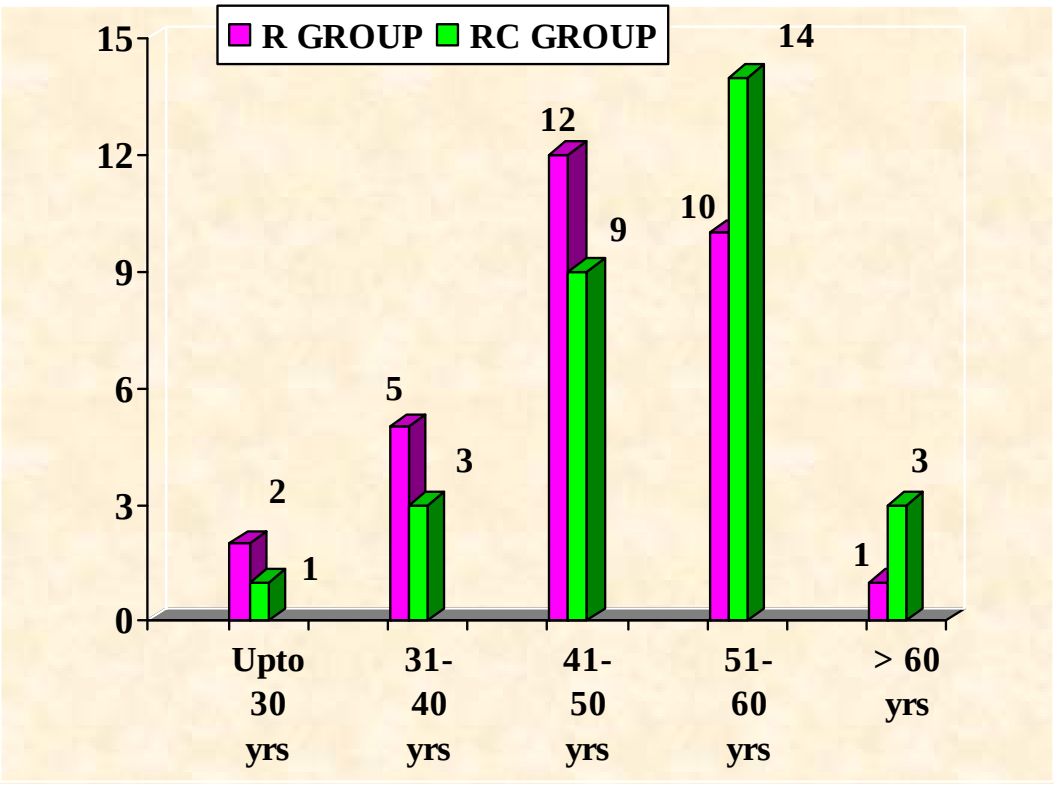
OBSERVATION AND RESULTS

1. AGE

Age group	Ropivacaine group		Ropivacaine & Clonidine group	
	No	**%**	**No**	**%**
Upto 30 years	2	6.7	1	3.3
31-40 years	5	16.7	3	10
41-50 years	12	40	9	30
51-60 years	10	33.3	14	46.7
Above 60	1	3.3	3	10
Total	30	100	30	100
Range	25-65 years		30-65 years	
Mean	48 years		51 years	
SD	9.4 years		8.5 years	
'p'	**0.173 NOT SIGNIFICANT**			

Age distribution in the group R varied from 25-65 years with mean age of 48 years and standard deviation of (9.4). In group RC age varied from 30 to 60 years with mean value of 51 years and standard deviation of (8.5) with a "p" value of 0.173 which is statistically insignificant.

AGE DISTRIBUTION

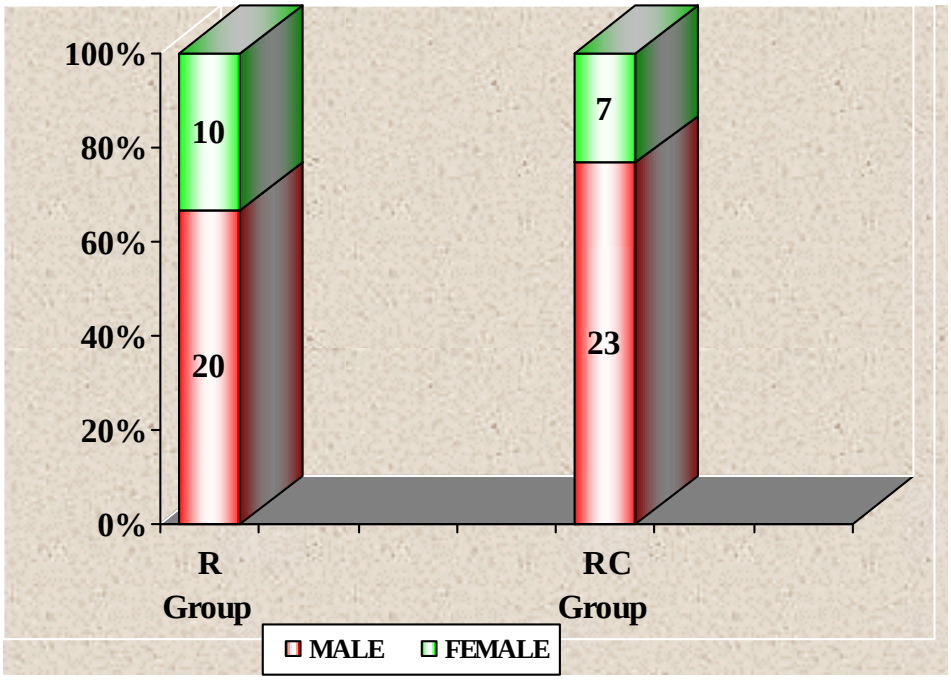


2. SEX DISTRIBUTION

Sex	Ropivacaine group		Ropivacaine & Clonidine group	
	No	**%**	**No**	**%**
Male	20	66.7	23	76.7
Female	10	33.3	7	23.3
Total	30	100	30	100
'p'	**0.5667 Not significant**			

In group R 20 patients were male 10 patients were female. In group RC 23 patients were male and 7 patients were female. There was no statistically significant difference in the sex composition of the two groups ("p" = 0.5667).

SEX DISTRIBUTION

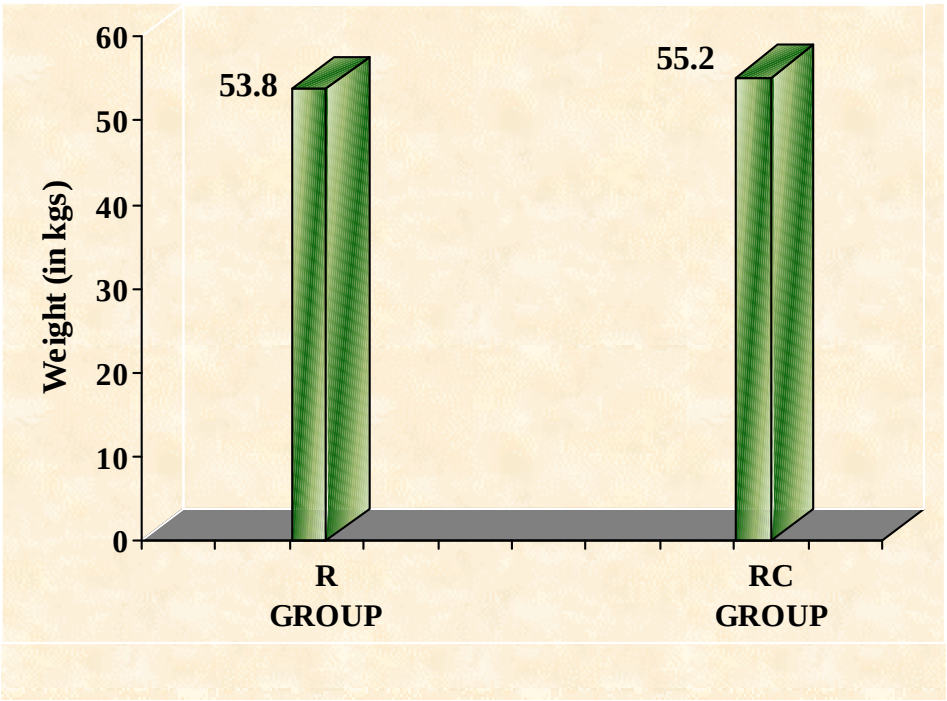


3. WEIGHT

Parameter	Weight (in kgs)	
	Ropivacaine group	**Ropivacaine & Clonidine group**
Range	40-70	45-70
Mean	53.8	55.2
SD	7.1	5.9
'p'	**0.4329 Not significant**	

Weight of the patients in the group R had a mean value of 53.8kgs with standard deviation of 7.1. In group RC had a mean value of 55.2 kgs with standard deviation of 5.9 with a "p" value of 0.4329 which is statistically insignificant.

WEIGHT

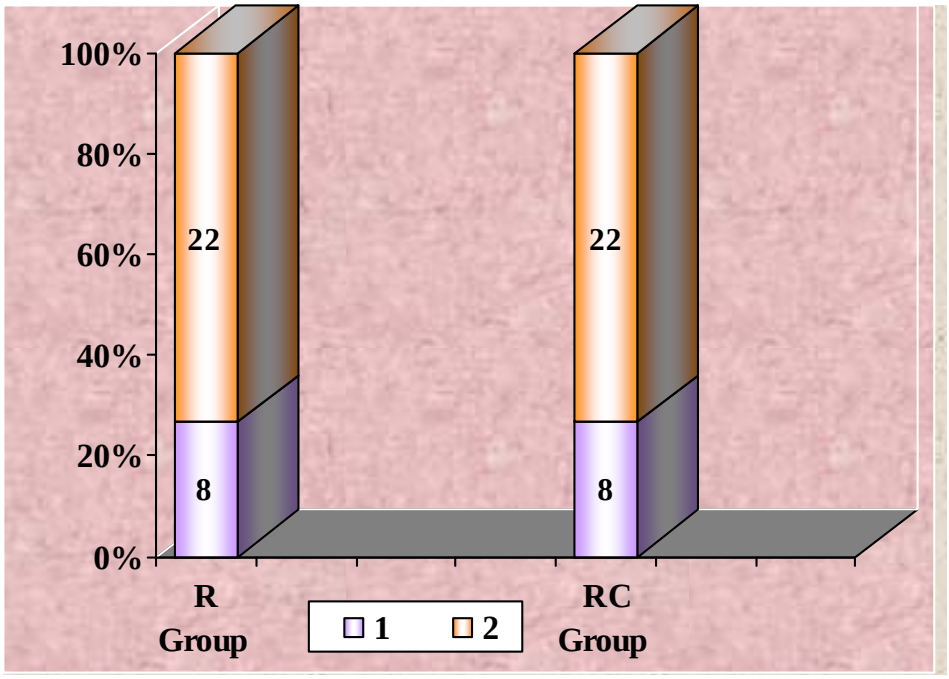


4. ASA STATUS

ASA	Ropivacaine group		Ropivacaine & Clonidine group	
	No	**%**	**No**	**%**
I	8	26.7	8	26.7
II	22	73.3	22	73.3
Total	30	100	30	100
'p'	**1.0 Not significant**			

In group R, 8 patients were ASA I and 22 patients were ASA II. In Group RC, 8 patients were ASA I and 22 patients were ASA II . Both the groups were comparable in respect to ASA classification with a "p" value of 1.0 which is statistically insignificant.

ASA



5. ONSET OF SENSORY BLOCK

Onset of sensory block	Group R (minutes)	Group RC (minutes)
Range	7-12	8-14
Mean	9.93	10.53
SD	1.6	1.8
P	**0.2605 Not significant**	

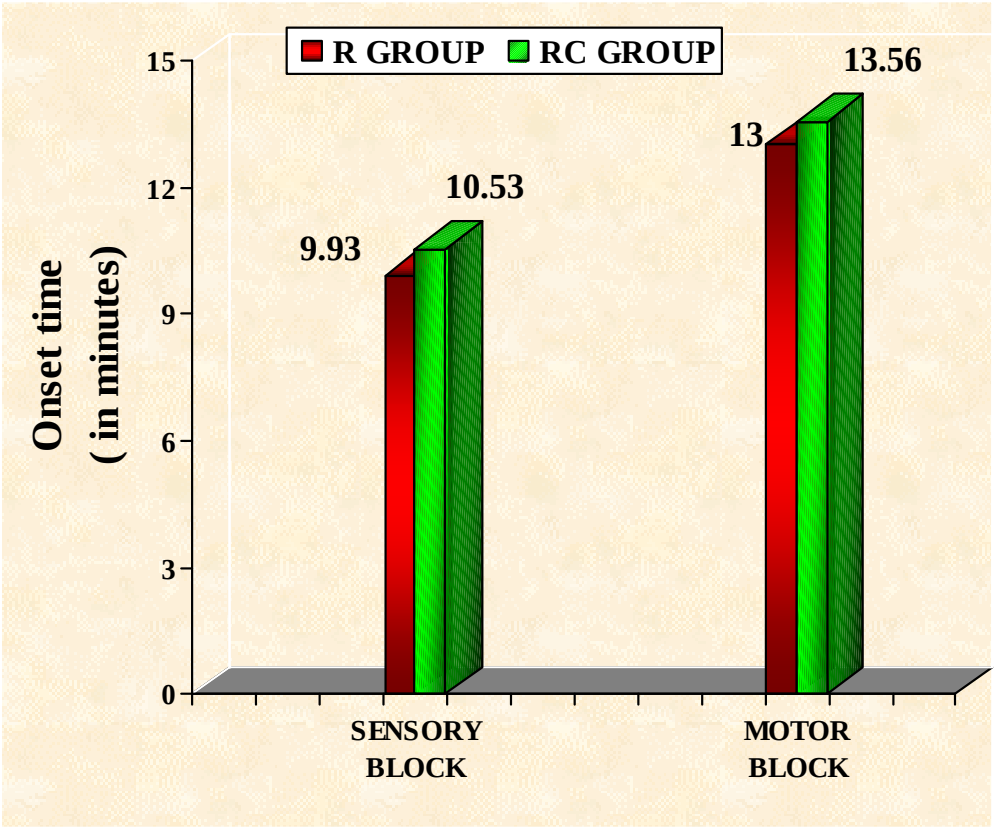
Time taken for the onset of sensory blockade in group R varied from 7 to 12 minutes with standard deviation of 1.6 . In group RC it varied from 8 to 14 minutes with standard deviation of 1.8 with a "p" value of 0.2605 which is statistically insignificant

6. ONSET OF MOTOR BLOCK

Onset of motor block	Group R (minutes)	Group RC (minutes)
Range	10-15	10-18
Mean	13.0	13.56
SD	1.2	1.96
'p'	**0.1414 Not significant**	

Onset of motor block varied from 10 to 15 minutes with standard deviation of 1.2. In group RC it varied from 10 to18 minutes with standard deviation of 1.96 with a "p" value of 0.1414 which is statistically insignificant.

ONSET OF SENSORY & MOTOR BLOCKS



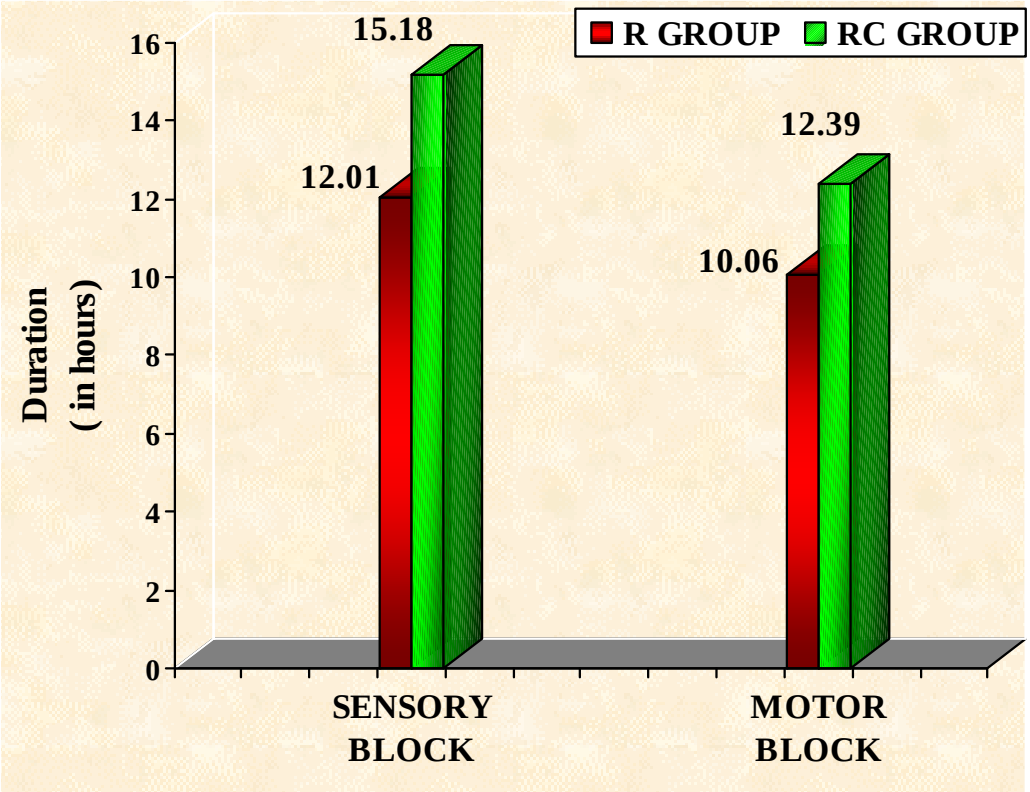
7. DURATION OF SENSORY AND MOTOR BLOCK

Parameter	Duration (in hours) of			
	Sensory block		Motor block	
	Ropivacaine group	Ropivacaine & Clonidine group	Ropivacaine group	Ropivacaine & Clonidine group
Range	10-13	14-16.5	9-11.8	11.5 – 14
Mean	12.01	15.18	10.06	12.69
SD	0.9	0.78	0.82	0.89
'p'	**0.0001 Significant**		**0.0001 Significant**	

Duration of sensory block in the Ropivacaine group was 12.01 $\pm$0.9 hours and in the Ropivacaine & clonidine group it was 15.18 $\pm$0.78 hours. Similarly duration of motor blocks in the two groups were 10.06 $\pm$0.82 hours and 12.69 $\pm$0.89 hours.

The differences between the two groups were **statistically significant** in respect to duration of sensory blockade with a "p" value of 0.0001 and the duration of motor blockade with a "p" value of 0.0001.

DURATION OF SENSORY & MOTOR BLOCKS

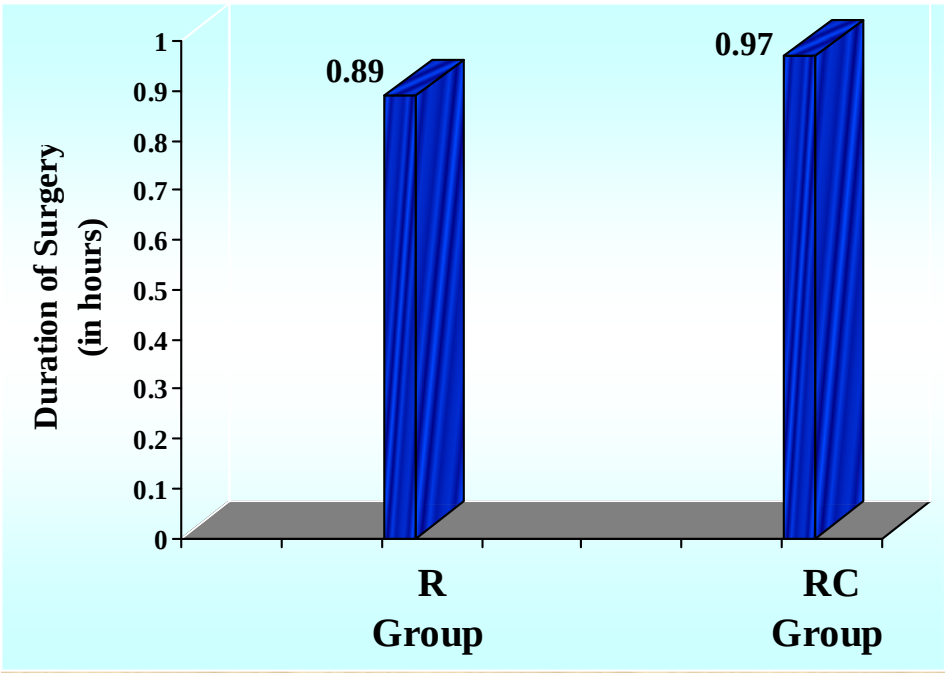


8. DURATION OF SURGERY

Parameter	Duration of surgery(in hours)	
	Ropivacaine group	**Ropivacaine & Clonidine group**
Range	0.58-1.15	0.67-1.5
Mean	0.89	0.97
SD	0.14	0.29
'p'	**0.8607 Not significant**	

There was no significant difference in the duration of surgery in the two groups ($p > 0.05$).

DURATION OF SURGERY

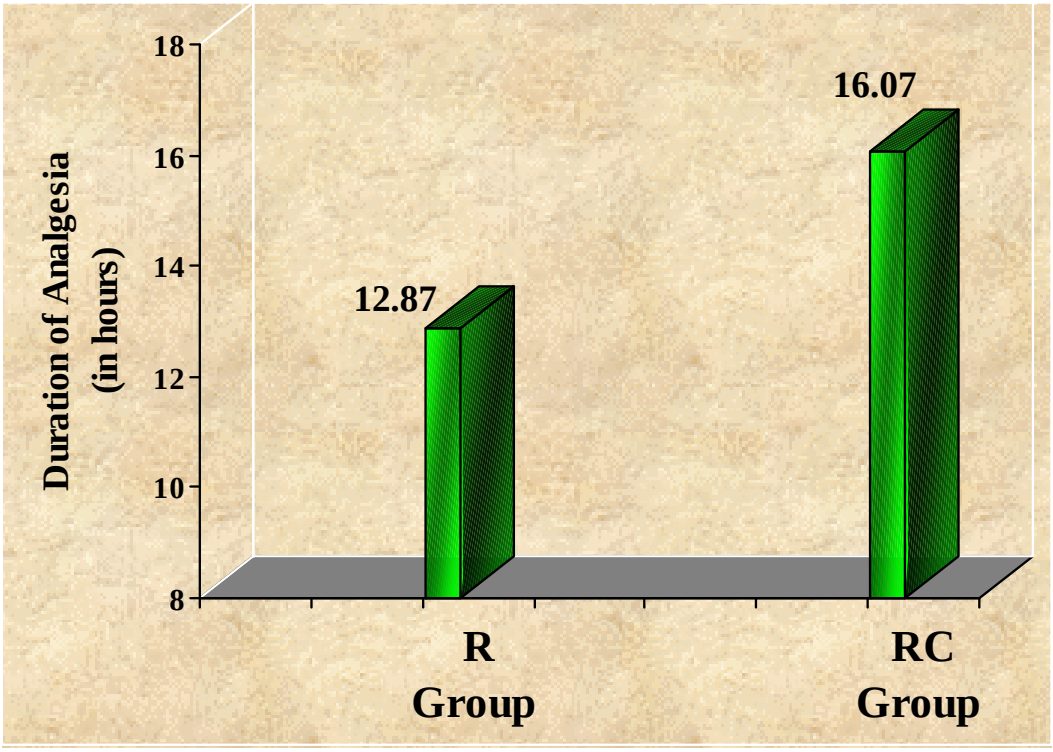


9. DURATION OF ANALGESIA

Parameter	Duration of analgesia (in hours)	
	Ropivacaine group	**Ropivacaine & Clonidine group**
Range	12-14	15-17.5
Mean	12.87	16.07
SD	0.63	0.68
'p'	**0.0001 Significant**	

Duration of analgesia was significantly longer in the Ropivacaine - Clodinine group (16.07 $\pm$0.68 hours) than in the Ropivacaine group (12.87 $\pm$0.67 hours). 'p' value was 0.0001. The difference between the two groups were **statistically significant**

DURATION OF ANALGESIA



10. SEDATION SCORE

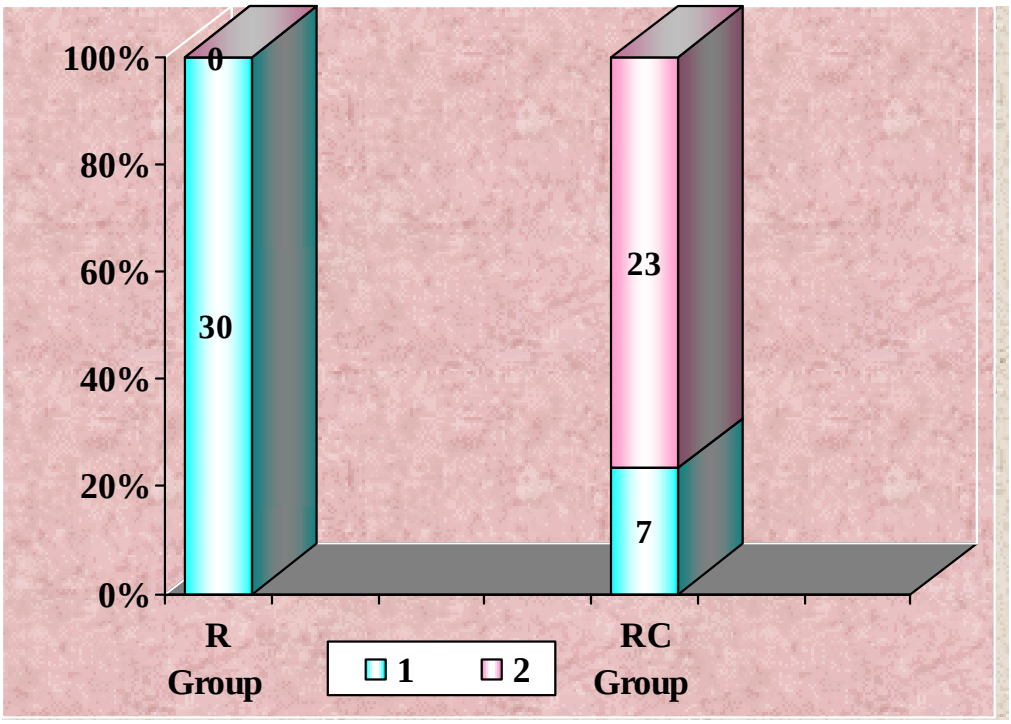
TABLE – 10: SEDATION SCORE

Sedation score	Ropivacaine group		Ropivacaine & Clonidine group	
	No	**%**	**No**	**%**
1	30	100	7	23.13
2	-	-	23	76.7
Total	**30**	**100**	**30**	**100**

All the cases in the Ropivacaine group had a sedation score of 1. But only 7 cases in Ropivacaine & Clodinine group had a score of 1 and the remaining 23 had a score of 2.

The difference between the two groups is **statistically significant** with a "p" value of 0.0001.

SEDATION SCORE

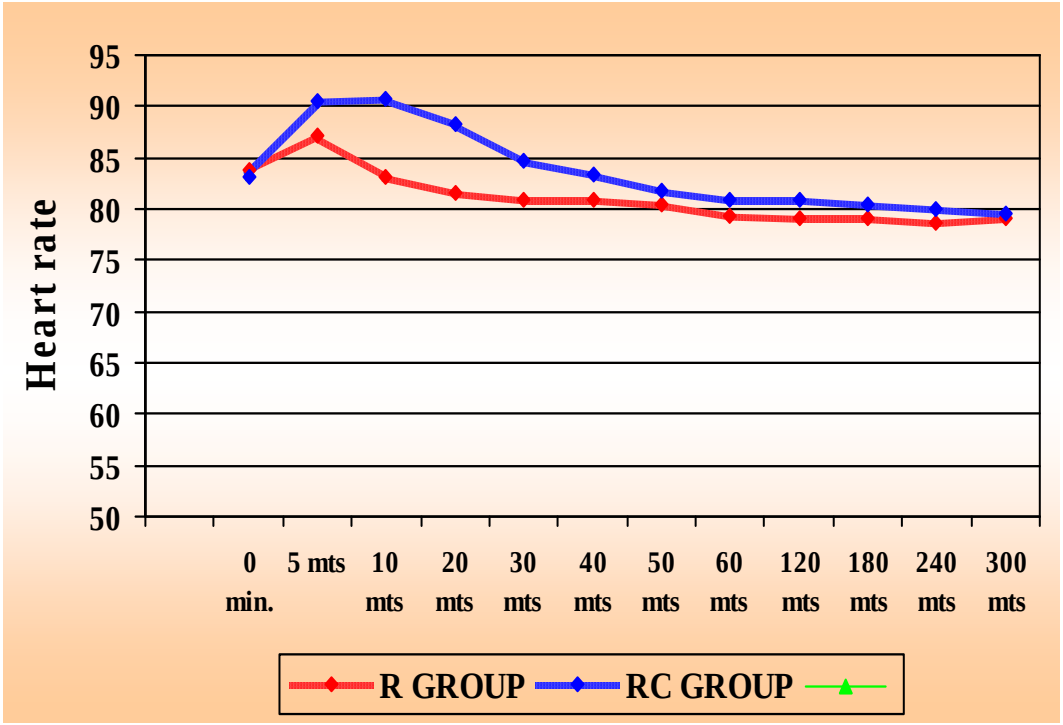


11. HEART RATE

Heart rate at	Heart rate (Mean ±SD) for		'p'	Significance
	Ropivacaine group	Ropivacaine & Clodinine group		
0 minute	83.9 ±11.9	83.2 ±12.2	0.7159	Not significant
5 minutes	87.1 ±11.9	90.5 ±13.2	0.1336	Not significant
10 minutes	83.1 ±11.8	90.7 ±13.3	0.0604	Not significant
20 minutes	81.5 ±11.6	88.2 ±12.5	0.0577	Not significant
30 minutes	81.0 ±10.7	84.8 ±12.7	0.1402	Not significant
40 minutes	80.9 ±10.1	83.3 ±12.6	0.4408	Not significant
50 minutes	80.5 ±10.8	81.7 ±12.0	0.5581	Not significant
60 minutes	79.4 ±10.0	80.9 ±11.7	0.5289	Not significant
120 minutes	79.1 ±9.8	81.0 ±11.8	0.4497	Not significant
180 minutes	79.1± 9.6	80.5 ±12.0	0.6617	Not significant
240 minutes	78.7 ±9.6	79.9 ±11.8	0.6176	Not significant
300 minutes	79.1 ±9.2	79.6 ±11.7	0.9467	Not significant

There were no statistically significant differences in the mean heart rates at all time intervals.

CHANGES IN HEART RATE

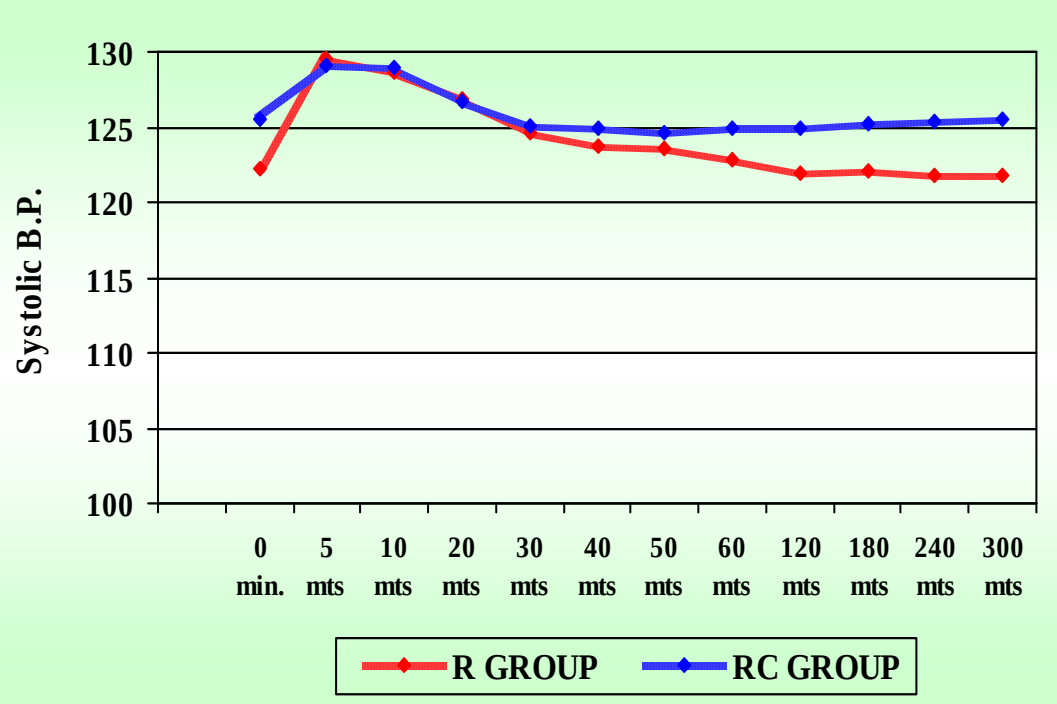


13. SYSTOLIC BLOOD PRESSURE

SBP at	SBP values (Mean ±SD) for		'p'	Significance
	Ropivacaine group(mmhg)	Ropivacaine & Clonidine group(mmhg)		
0 minute	122.3 ±10.7	125.5 ±9.7	0.2625	Not significant
5 minutes	129.5 ±8.8	129.1 ±9.5	0.8928	Not significant
10 minutes	128.7±9	129 ±9.3	0.7429	Not significant
20 minutes	126.8 ±10.1	126.7 ±9.1	0.9583	Not significant
30 minutes	124.7± 10.1	125.1± 10	0.749	Not significant
40 minutes	123.8 ±10.0	124.9 ±9.7	0.7042	Not significant
50 minutes	123.6 ±10.3	124.7 ±10.1	0.6651	Not significant
60 minutes	122.9 ±10.2	124.9 ±9.8	0.4923	Not significant
120 minutes	122.0 ±10.5	125 ±9.6	0.3207	Not significant
180 minutes	122.1 ±10.1	125.2 ±9.4	0.2726	Not significant
240 minutes	121.8 ±10.5	125.3 ±9.7	0.2252	Not significant
300 minutes	121.8 ±10.5	125.5 ±9.6	0.1778	Not significant

Mean systolic blood pressure of the two groups did not have a any significant difference at all time intervals.

CHANGES IN SYSTOLIC B.P.

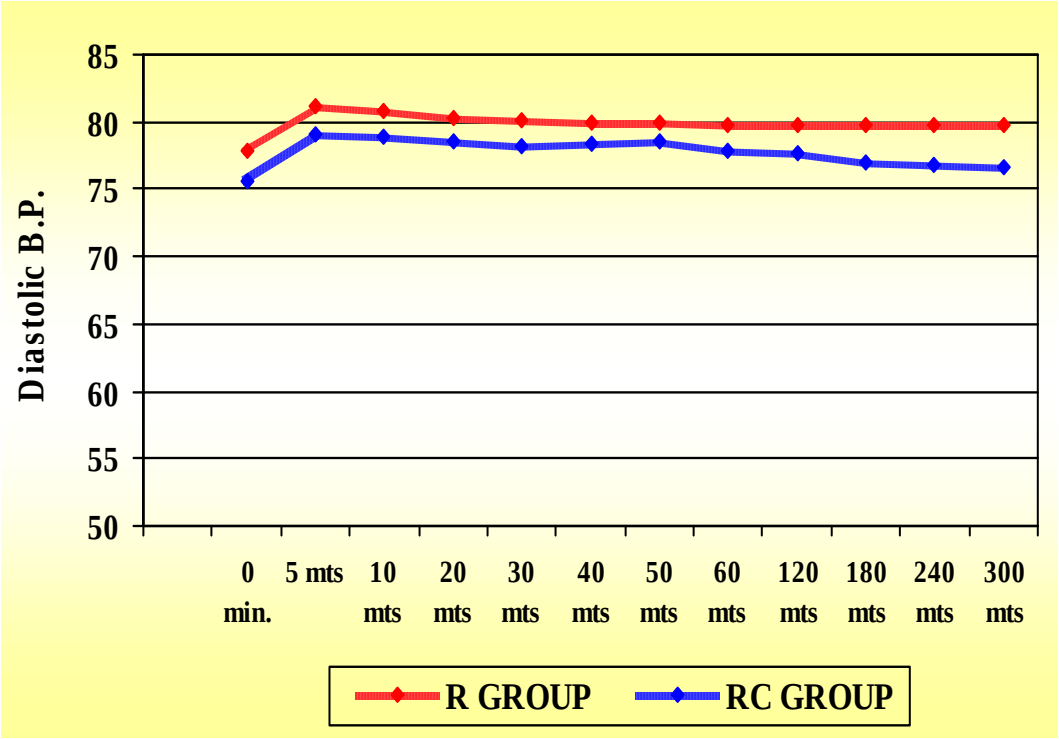


14. DIASTOLIC BLOOD PRESSURE

DBP at	DBP values (Mean ±SD) for		'p'	Significance
	Ropivacaine Group (mmhg)	Ropivacaine & Clodinine Group (mmhg)		
0 minute	77.9 ±6.7	75.6± 5	0.1273	Not significant
5 minutes	81.1 ±7.3	79.1 ±6.3	0.3564	Not significant
10 minutes	80.9 ±6.3	78.9 ±6.3	0.3287	Not significant
20 minutes	80.3 ±6.5	78.5 ±6.7	0.3797	Not significant
30 minutes	80.1 ±6.6	78.2 ±6.8	0.3815	Not significant
40 minutes	80.0 ±6.2	78.4 ±7	0.3944	Not significant
50 minutes	79.9 ±6.3	78.5 ±6.9	0.4543	Not significant
60 minutes	79.8 ±6.2	77.9 ±6.6	0.3402	Not significant
120 minutes	79.8 ±6.2	77.6 ±6.6	0.2607	Not significant
180 minutes	79.7 ±6.1	77.0 ±6.7	0.1887	Not significant
240 minutes	79.7 ±6.3	76.8 ±6.8	0.144	Not significant
300 minutes	79.7 ±6.3	76.7 ±6.8	0.0949	Not significant

There were no statistically significant differences in the mean diastolic blood pressures of two groups at all time intervals.

CHANGES IN DIASTOLIC B.P.

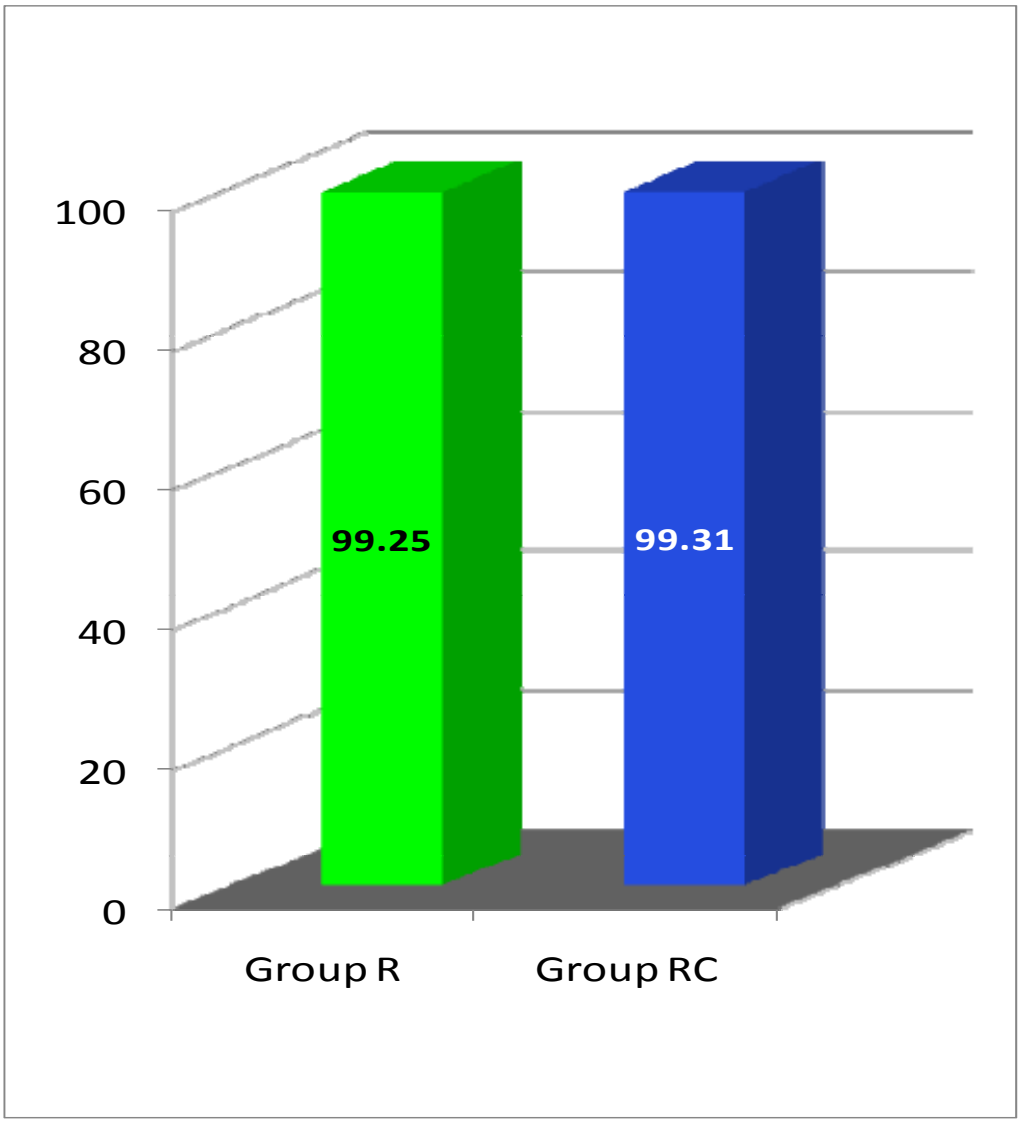


15. SATURATION

Parameter	SPO2 %	
	Ropivacaine group	**Ropivacaine & Clonidine group**
Range	98.4-100	98.6-99.9
Mean	99.25	99.31
SD	0.54	0.45
'p'	**0.7768 Not Significant**	

Differences in the mean SpO_2 values of the two groups were 99.25 and 99.31 with a "p" value of 0.7768 which is statistically insignificant.

SPo_2



DISCUSSION

Alpha- 2agonist like clonidine assumes greater importance as anaesthetic adjuvant and analgesic. Its primary effect is symphatholytic. It reduces peripheral norepinephrine release by stimulation of prejunctional inhibitory alpha-2 adrenoreceptors. It inhibits central neural transmission in the dorsal horn by presynaptic and postsynaptic mechanism and directly in spinal preganglionic sympathetic neurons. Tradionally it was used as antihypertensive drug, but uses based on sedative, anxiolytic and analgesic properties are being developed.

In this study 60 microgram of clonidine added to combined sciatic femoral block has showed no statistically significant difference between the two groups as regard to age, sex, weight and ASA status. Onset of sensory and motor blocks occurred in 9.93 $\pm$1.6 minutes and 13 $\pm$1.2 minutes respectively in the ropivacaine group. Onset of sensory and motor block occurred in 10.53 $\pm$ 1.8 minutes and 13.56 $\pm$ 1.96 minutes in the ropivacaine clonidine group. The addition of clonidine has not shown much effect on the onset of sensory and motor block. Duration of surgery was comparable in both groups.

Mean duration of sensory block in ropivacaine group was 12.01$\pm$ 0.9 hours and in ropivacaine clonidine group was 15.18$\pm$ .78 hrs. The

difference between the two groups was **statistically significant** with a p value of 0.0001 (P<0.05).

These results correlates with studies conducted by casti et all, in which the duration of sensory block was 10-13 hours in ropivacaine group and it was 12-16 hours in ropivacaine clonidine group.

Mean duration of motor block in ropivacaine group was 10.06 ±0.82 hours and in ropivacaine clonidine group was 12.69 ±0.89 hours. The difference between the two groups was **statistically significant** with a p value of 0.0001 (P<0.05). These results correlates with studies conducted by casti et all, in which the duration of motor block was 8-14 hours in ropivacaine group and it was 8.5-22 hours in ropivacaine clonidine group. The addition of clonidine to local anaesthetic solution has significantly prolonged the duration of sensory and motor blockade. This is because clonidine blocks the conduction of C and A gamma fibres and increase the potassium conductance in isolated neurons and intensifies the conduction of local anesthetics.

Duration of analgesia was significantly longer in the ropivacaine - clodinine group (16.07 ±0.68 hours) than in the ropivacaine group (12.87 ±0.67 hours). The difference between the two groups was **statistically significant** with a p value of .0001<(p0.05). These results correlates with

studies conducted by casti et all, in which duration of analgesia was 11.8-14.5 hours in ropivacaine group and it was 13.5-17.8 hours in ropivacaine clonidine group. Clonidine has been demonstrated to inhibit the action potential of A- alpha and C fibres in desheathed sciatic nerves. The α2 adrenergic receptors activated by clonidine are located on primary afferent terminals, neurons in the superficial laminae of the spinal cord and in brain stem nuclei implicated in analgesia. Inhibition of noradrenaline release, mediated by an interaction with α2 adrenergic presynaptic receptors is responsible for the enhancing effect of the peripheral administration of clonidine. Peripheral antinociception induced by clonidine has also been related to an α2- adrenorecptor mediated local release of enkephalin like substance.

The sedation score in both groups are noted. The sedation score in ropivacaine group was 1.0, in ropivacaine clonidine group was 2.4± 0.5. The sedation score between the two groups was **statistically significant** with a "p" value of 0.0001. In clonidine group since the sedation score was not more than 3, the respiratory function was not compromised.

In this study, no significant difference was observed with respect to the pulse rate, systolic and diastolic blood pressure and saturation.

By performing sciatic femoral nerve block for lower limb surgeries, adequate postoperative analgesia can be given. Pain is an important factor for any cardiovascular disease patients undergoing surgery in the lower limb. Postoperative pain produces tachycardia, which could be deleterious to the patients. Hence sciatic femoral nerve block can be performed for these cardiovascular disease and high risk patients that can provide prolonged postoperative analgesia and comfort to the patient. . Clonidine like adjuvants will prolong the duration of postoperative analgesia. Low dose of clonidine produces sedation without any respiratory compromise. Hence the addition of low dose of clonidine in nerve blocks will provide sedation and prolongation of postoperative analgesia without any systemic side effects.

SUMMARY

60 Patients of ASA grade I or II undergoing upper limb surgeries were randomly assigned into two groups, groups R and RC.

Surgery was done under sciatic femoral nerve block through Labats approach. The patients in group R received 30 ml at 0.75% Ropivacaine and 0.4 ml Normal saline. In group RC received 30 ml at 0.75% Ropivacaine and 60 micrograms clonidine. In this 30ml mixture, 18 ml given in sciatic nerve block and 12 ml given in femoral nerve block.

Parameters observed were time of onset of sensory and motor block, duration of motor blockade, and sensory blockade, duration of post operative analgesia, sedation score and side effects.

This study shows that

1. There is no significant difference in the onset of sensory blockade in ropivacaine clonidine group when compared to ropivacaine
2. There is no significant difference in the onset of motor blockade in ropivacaine clonidine group when compared to ropivacaine
3. Duration of sensory block in the ropivacaine group was 12.01 hours and in the ropivacaine clonidine group was 15.18 hours. The addition of clonidine to ropivacaine increases the duration of sensory blockade by 184 minutes,when compared to ropivacaine alone.

4. Duration of motor block in ropivacaine was 10.06 hours and in ropivacaine clonidine was 12.69 hours. The addition of clonidine to ropivacaine increases the duration of motor blockade by 157 minutes.
5. Duration of analgesia in ropivacaine group was 12.87 hours and in the ropivacaine clonidine group was 16.07 hours. The addition of clonidine to ropivacaine significantly prolongs the duration of post operative analgesia by 192 minutes when compared to ropivacaine alone.
6. In ropivacaine group the mean intraoperative sedation score was 1.In clonidine group, the mean intraoperative sedation score was 1.76 which did not compromise respiratory function.
7. There were no side effects like hypotension and bradycardia in clonidine group.

CONCLUSION

The addition of clonidine to ropivacaine in sciatic femoral nerve block shows no difference in the onset of sensory and motor blockade but prolongs the duration of both sensory and motor blockade and post operative analgesia, when compared to ropivacaine alone.

BIBLIOGRAPHY

1. Ronald D. Miller. Pharmaeology of local anaesthetics 2010 7th 913.
2. Alfred Goodman and Gilman the pharmacology in Basis of therapeutics 1996;5(9);848-856.
3. William F.Ganong Review of medical physiology 2001;20;49 -61.
4. K.D.Tripathi Essentials of medical pharmacology local Anesthetics 2008 6th ed;(350 -361).
5. Casati A, Borghi B, Fanelli G, et al. Ropivacaine or 2% mepivacaine for lower limb peripheral nerve blocks. *Anesthesiology* 1999;**90**:1047-1053
6. Greengrass RA, Klein SM, D'Ercole JF, et al. Lumbar plexus and sciatic nerve block for knee arthroplasty: comparison of ropivacaine and bupivacaine. *Can J Anaesth* 1998; **45**:1094–6.
7. Gaumann DM, Brunet PC, Jirounek P. Hyperpolarizing after potentials in C fibers and local anesthetic effects of clonidine and lidocaine. Pharmacology 1994; 48:21–9.
8. Casati A, Fanelli G, Cappelleri GL, et al. A clinical comparison of 0.75% ropivacaine, 1% ropivacaine or 0.5% bupivacaine for interscalene brachial plexus anaesthesia. Eur J Anaesth 1999;16:784–9.

9. Eisenach JC, De Kock M, Klimsha W. a2-Adrenergic agonists for regional anesthesia: a clinical review of clonidine. Anesthesiology 1996; 85:655–74.
10. Nakamura M, Ferreira SH. Peripheral analgesic action of clonidine: medication by release of endogenous enkephalin-like substances. Eur J Pharmacol 1988;146:223– 8.
11. Casati A, Fanelli G, Beccaria P, et al. Effects of the single or multiple injection technique on the onset time of peripheral nerve blocks with 0.75% ropivacaine. Anesth Analg 2000;91:181–4
12. Harold Ellis, stanly Feldman, Anatomy for anaesthetic1997;160 -195
13. Grays anatomy for students 2010.
14. Danilo Jan kovic Regional Nerve Blocks and Infiltration Therapy
15. Text book of regional anesthesia p.prithiviraj .
16. Fanelli G. Peripheral nerve block with electric neurostimulation. Miner Anestesiol 1992;58:1025-6.
17. Markham A, Faulds D. Ropivacaine: a review of its pharmacology and therapeutic use in regional anaesthesia. Drugs 1996;52: 429-49.
18. Robert K.Stoelting pharmacology and physiology in anaesthetic practice, 4thed: 340 -344.

19. Coylic and Churchill Davidson's, A practice of anaesthesia, 7th edition 60+, Adjuvants to local anesthetics.
20. Therapeutical pharmacology- Churchill livingstone C-294-296, R 54-57

PROFORMA

TO EVALUATE THE EFFECTIVENESS OF CLONIDINE AS AS AN ADJUVANT TO ROPIVACAINE IN SCIATIC FEMORAL NERVE BLOCK FOR LOWER LIMB SURGERY

Name : Age: Sex: ASA status:

IP No : Weight:

Diagnosis :

Surgery :

Investigations

Hb %:

Urine Albumin:

Sugar:

Blood sugar:

Blood urea: – mg%

Serum creatinine: mg%

Group R – 30 ml of 0.75% Ropivacaine + 0.4 ml NS

Group RC – 30 ml of 0.75% Ropivacaine + 150 microgram clonidine

OBSERVATIONS

Onset of sensory blockade :

Onset of motor blockade :

Duration of sensory blockade :

Duration of motor blockade :

Duration of surgery :

Duration of analgesia :

Side effects

Hypotension : yes/no Bradycardia: yes/no

Motor block

0 – Normal power

1 - Paresis but able to move arm

2 - Not able to move arm but able to move fingers

3 - Complete motor blockade.

VAS (Visual analog scale):

Sedation score: Ramsay sedation score

1. Awake and alert
2. Conscious and oriented
3. Sedated responding to verbal stimulus
4. Responding to mild physical stimulus
5. Responding to moderate and severe physical stimulus
6. Arousable.

GROUP - ROPIVACAINE

Sl. No	Name	Age/ Sex	IP NO	Wt in Kg	ASA Status	Diagnosis & Procedure	onset of Sensory block in Mins.	onset of Motor block in Mins	Duration of sensory block in Hrs.	Duration of Motor block in Hrs.	Duration of analgesia	Duration of surgery in Hrs	Sedation score	Side effects
1	Indumathy	54/F	73451	55	II	Right diabetic foot-BK Amputation	6	8	12.5	10	13.1	0.75	1	nil
2	Rajappan	46/M	6071	60	II	PVOD left foot- BK Amputation	8	12	12.8	10.5	13.5	1	1	nil
3	Arumugam	25/M	46682	50	I	Metatarsal fracture -k wire fixation	7	10	11	9	12.2	1	1	nil
4	Arumugam	60/M	6157	55	II	Left diabetic foot-BK Amputation	8	9	12.5	10.5	13.5	0.833333	1	nil
5	Pandiammal	50/F	2756	45	II	Right diabetic foot-BK Amputation	6	10	12.8	10.8	14	1	1	nil
6	Murugan	25/M	92448	60	I	Left diabetic foot-BK Amputation	8	10	12.8	10	13	1.15	1	nil
7	Ravichandran	40/M	44417	60	II	Right diabetic foot-BK Amputation	10	12	12	10	12.8	1	1	nil
8	Jeyalakshmi	45/F	48676	50	II	Right diabetic foot-BK Amputation	12	14	12.5	11	13	1.15	1	nil
9	Ramalingam	50/M	32245	50	II	PVOD left foot -BK Amputation	8	12	12.8	10.5	13.2	1	1	nil
10	Karuppiah	55/M	24951	60	II	Left diabetic foot-BK Amputation	8	10	11	9	12	0.75	1	nil
11	Suraj	36/M	42780	50	I	PVOD right foot -BK Amputation	9	14	12	11	12.5	0.833333	1	nil
12	Kumar	44/M	44082	70	II	Right diabetic foot-BK Amputation	12	14	12.5	10	13	0.75	1	nil
13	Chinnakannu	60/M	4908	50	II	PVOD right leg-BK Amputation	10	12	10	9	12	0.83333	1	nil
14	Sonnaiammal	55/F	39214	60	II	PVOD right leg-BK Amputation	8	10	12.5	10	12.2	1	1	nil
15	Raju	40/M	56811	60	I	Right diabetic foot-BK Amputation	10	14	12.8	11	13.5	0.75	1	nil
16	Palaniappan	56/M	61259	45	II	Left diabetic foot-BK Amputation	8	12	13	11	13.5	0.83333	1	nil
17	Tamilarasi	50/F	19362	50	I	Left diabetic foot-BK Amputation	7	10	11	9	12.5	1	1	nil
18	Ponnuthai	60/F	19711	40	II	Right diabetic foot-BK Amputation	8	9	12.5	10.5	13	0.83333	1	nil
19	Ganapathi	56/M	70576	60	II	Metatarsal fracture -k wire fixation	8	10	12.8	10.8	14	1	1	nil
20	Muthukrishnan	40/M	6948	62	I	Lateral malleolus fracture- k-wire fixation	10	12	10	9	12	0.83333	1	nil
21	Raja	48/M	78910	55	II	Non healing ulcer-rt foot-BK Amputation	12	14	12.5	10	13	0.83333	1	nil
22	Mohammed ali	50/M	41505	65	II	Cellulitis right foot-BK Amputation	10	12	12	10	12.5	1	1	nil
23	Indirani	38/F	76608	42	I	Left diabetic foot-BK Amputation	9	14	11.5	9	12	0.75	1	nil
24	krishnaveni	52/F	57682	50	II	PVOD right leg-BK Amputation	8	10	12.5	11	13.5	1	1	nil
25	Balu	44/M	22526	50	II	Right diabetic foot-BK Amputation	8	12	12.5	11.8	13.8	0.75	1	nil
26	Ganesan	46/M	70770	50	II	PVOD right leg- BK Amputation	10	12	10	9	12	0.83333	1	nil
27	Sundaram	65/M	2501	50	II	PVOD left leg- BK Amputation	12	14	12	10	12.8	0.583333	1	nil
28	Subramanian	50/M	14389	45	I	Crushinjury right foot- stabilisation	7	9	11	9	12	0.75	1	nil
29	Pandian	48/M	32385	50	II	Left diabetic foot-BK Amputation	9	13	12	9	13	0.833333	1	nil
30	Dhanalakshmi	52/F	36907	55	II	Right diabetic foot-BK Amputation	10	12	12.5	10.5	13	1	1	nil

GROUP ROPIVACAINE PULSE RATE CHART(beats/min)

S.No.	GROUP	0 MIN	5 MIN	10 MIN	20 MIN	30 MIN	40 MIN	50 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN
1	R	90	95	96	92	90	84	86	84	84	84	84	84
2	R	110	112	114	112	110	106	104	102	102	100	102	100
3	R	100	110	98	96	94	94	96	94	92	92	92	92
4	R	78	75	74	74	76	74	72	72	70	72	70	72
5	R	84	82	84	82	80	78	78	76	74	72	74	74
6	R	114	116	110	108	106	104	104	102	100	99	98	98
7	R	114	108	104	104	102	102	104	100	98	98	98	98
8	R	82	86	78	76	78	80	82	80	78	78	78	78
9	R	88	94	96	92	90	90	90	88	88	86	86	84
10	R	84	88	88	84	84	82	82	80	82	84	84	84
11	R	74	80	78	76	77	76	74	74	72	76	72	72
12	R	84	80	78	76	76	76	74	72	74	74	72	72
13	R	78	74	72	72	76	76	76	78	76	72	72	72
14	R	74	80	70	68	68	68	66	68	68	68	66	66
15	R	88	84	82	82	80	80	84	82	78	80	80	80
16	R	78	84	78	74	72	74	72	70	72	70	72	78
17	R	80	86	78	80	76	76	74	76	76	76	74	74
18	R	78	80	78	76	74	76	74	72	70	70	72	72
19	R	82	86	80	78	76	77	78	79	80	84	80	80
20	R	86	90	87	89	88	88	88	86	84	84	82	82
21	R	78	84	80	76	78	75	74	72	74	72	70	70
22	R	80	84	78	78	80	82	76	77	78	80	78	78
23	R	72	78	76	74	72	77	78	78	76	79	72	72
24	R	74	78	72	70	70	72	68	66	68	70	72	72
25	R	76	80	76	74	75	76	75	76	75	74	72	72
26	R	77	80	76	75	75	74	72	74	72	70	72	74
27	R	70	74	72	70	72	76	78	74	72	72	72	74
28	R	80	84	78	76	76	74	74	72	74	72	78	78
29	R	70	74	68	69	70	67	68	67	69	70	72	74
30	R	94	106	94	92	90	94	94	92	97	96	94	96

GROUP ROPIVACAINE SYSTOLIC BLOOD PRESSURE(mmhg)

S.No	GROUP	0 MIN	5 MIN	10 MIN	20 MIN	30 MIN	40 MIN	50 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN
1	R	130	128	130	130	130	130	130	130	130	130	130	130
2	R	140	146	144	140	140	140	140	140	140	140	140	140
3	R	120	130	130	128	120	120	120	120	120	120	118	118
4	R	120	120	124	120	118	118	120	120	120	120	120	120
5	R	130	130	134	134	128	128	128	126	120	128	128	128
6	R	140	140	138	138	138	138	140	140	140	140	140	140
7	R	120	124	124	128	128	128	128	120	120	120	120	120
8	R	120	124	120	120	120	120	118	118	118	118	120	120
9	R	130	130	130	128	128	128	130	130	130	130	130	130
10	R	120	130	130	128	128	126	120	120	120	118	118	118
11	R	110	120	116	114	112	110	110	110	110	110	110	110
12	R	110	118	120	120	116	114	112	110	110	108	106	106
13	R	120	130	130	120	118	118	116	116	114	114	110	110
14	R	130	130	130	128	126	124	128	128	128	126	124	124
15	R	100	120	116	104	104	102	102	102	100	104	104	104
16	R	110	120	120	120	120	120	116	114	114	114	112	112
17	R	130	140	130	128	128	126	126	124	124	122	122	122
18	R	130	140	140	138	136	130	130	130	134	130	130	130
19	R	120	128	128	128	126	126	126	126	122	120	120	120
20	R	110	118	118	120	120	1220	120	116	110	116	116	116
21	R	140	146	148	150	144	144	144	142	140	140	142	142
22	R	120	130	130	130	130	128	128	128	124	124	124	124
23	R	130	136	136	136	136	132	130	130	130	130	130	130
24	R	130	134	134	134	132	132	130	130	130	130	130	130
25	R	110	120	120	120	110	110	110	112	112	112	110	110
26	R	120	128	126	126	126	124	126	124	120	120	120	120
27	R	110	116	116	110	110	110	110	110	110	110	110	110
28	R	120	130	130	118	118	118	120	120	120	120	120	120
29	R	140	148	148	146	140	140	140	140	140	140	140	140
30	R	110	130	120	120	110	110	110	110	110	110	110	110

GROUP ROPIVACAINE DIASTOLIC BLOOD PRESSURE(mmhg)

S.No	GROUP	0 MIN	5MIN	10 MIN	20 MIN	30MIN	40 MIN	50 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN
1	R	80	80	80	78	78	78	78	76	76	76	78	78
2	R	80	84	80	80	78	80	80	80	80	80	80	80
3	R	70	70	70	70	70	70	70	70	70	70	70	70
4	R	80	82	84	80	82	80	78	78	78	78	78	78
5	R	80	80	80	78	78	78	78	78	78	78	78	80
6	R	80	80	80	80	80	80	80	82	82	80	80	80
7	R	90	96	88	88	88	88	90	90	90	90	90	90
8	R	80	80	80	80	76	76	78	76	76	76	76	76
9	R	72	74	74	74	74	74	74	76	76	76	76	76
10	R	70	76	76	76	74	74	74	74	74	74	74	74
11	R	80	82	82	82	82	82	82	82	82	80	82	82
12	R	70	74	74	72	72	72	72	72	72	70	70	70
13	R	70	76	76	76	76	76	78	78	8	78	78	78
14	R	80	84	84	82	82	82	82	82	80	80	80	80
15	R	70	70	70	70	70	70	70	70	70	74	74	74
16	R	80	80	80	80	82	84	84	84	86	86	86	86
17	R	82	80	80	78	76	78	78	78	78	78	76	76
18	R	80	84	84	84	84	82	80	82	82	80	80	80
19	R	90	96	94	98	98	94	94	94	94	94	94	94
20	R	70	70	76	76	76	76	76	76	76	76	78	78
21	R	90	94	94	92	92	92	92	90	90	90	90	90
22	R	70	78	78	78	78	78	78	78	77	76	76	76
23	R	80	84	84	84	84	86	86	84	84	84	84	84
24	R	84	88	90	90	90	90	90	90	90	90	90	90
25	R	70	74	76	76	76	76	76	76	78	78	78	78
26	R	80	88	88	84	84	80	80	80	80	80	80	80
27	R	70	76	78	78	78	78	76	76	76	76	74	74
28	R	80	84	84	82	82	82	80	80	80	80	80	80
29	R	70	76	74	74	74	74	74	72	72	72	70	70
30	R	88	94	90	90	90	90	90	90	90	90	90	90

GROUP - ROPIVACAINE CLONIDINE

S. No	Name	Age/ Sex	IP NO	Wt in Kg	ASA	Diagnosis & Procedure	onset of Sensory block in Mins.	onset of Motor block in Mins	Duration of sensory block in Hrs.	Duration of Motor block in Hrs.	Duration of analgesia	Duration of surgery in Hrs	Sedation score	Side effects
1	Ayyavoo	50/M	15327	62	I	Left diabetic foot-BK Amputation	10	12	15.8	12	16.5	1.5	2	nil
2	Periammal	52/F	33177	55	II	Left diabetic foot-BK Amputation	9	14	15.5	11.8	16	0.75	1	nil
3	Vinayagham	58/M	38890	65	I	Crush injury right foot-k-wirestabilisation	10	14	16	14	17.5	1.5	2	nil
4	Rajendran	65/M	44664	50	II	Non healing ulcer-rt foot-BK Amputation	12	14	15.5	12	16.2	0.75	2	nil
5	Jayapal	55/M	87759	60	II	Right diabetic foot-BKAmputation	8	10	15	13	16	0.75	2	nil
6	Muthusamy	60/M	5695	50	II	Left diabetic foot-BK Amputation	9	13	14	11.5	15.2	1	2	nil
7	Solaimalai	52/M	37656	60	II	Right diabetic foot-BKAmputation	12	15	15	12	16.2	0.666667	2	nil
8	Perumal	48/M	104962	70	I	Left diabetic foot-BK Amputation	10	15	14	11.5	15	1.5	2	nil
9	Chellaiya	62M	678037	50	II	Right diabetic foot-BK Amputation	14	18	16.5	14	17	1	2	nil
10	Veerayee	42/F	36141	55	I	Bimalleolar fracture- k wire fixation	12	14	15.5	12	16.5	0.75	2	nil
11	Nataraj	55/M	75978	50	II	PVOD left foot -BK amputation	8	10	15	13	15.2	0.666667	1	nil
12	Occhammal	56/F	44070	60	II	Left diabetic foot-BK Amputation	9	12.8	14	11.5	15	1	2	nil
13	Raju	60/M	41814	60	II	PVOD-rightt foot -BK amputation	10	12	15.8	12	16.8	1.5	2	nil
14	Poomari	55/F	61918	60	II	Right diabetic foot-BK Amputation	12	14	15	13	16.2	1	2	nil
15	Manikkam	52/M	72791	50	II	PVOD right leg-BK Amputation	14	15	16.5	14	16.8	1.25	1	nil
16	Nataraj	34/M	101798	50	I	PVOD right leg-BK Amputation	10	12	15.5	12.5	16.5	1.5	1	nil
17	Pandi	50/M	38346	60	II	Right diabetic foot-BK Amputation	9	14	15	11.8	15.8	0.75	2	nil
18	Moideen beevi	55/F	38694	55	II	Left diabetic foot-BK Amputation	10	12	16	14	17.2	1	2	nil
19	Muthusamy	60/M	56957	50	II	Left diabetic foot-BK Amputation	12	14	15.5	12	16.5	0.75	1	nil
20	Bose	45/M	25340	60	II	Right diabetic foot-BKAmputation	10	15	14	11.5	15	1.25	2	nil
21	Shanmugam	48/M	46613	50	II	Metatarsal fracture -k wire fixation	8	10	14	13.5	15.8	1	2	nil
22	Shanthi	30/F	38890	50	I	Lateral malleolus fracture- k wire fixation	9	12	14	12	15.5	0.75	1	nil
23	Irulan	52/M	106427	55	II	Non healing ulcer-rt foot-BK Amputation	12	15	15	13	16.2	0.666667	2	nil
24	Vellaipandi	40/M	40125	50	I	Cellulitis right foot-BK Amputation	12	14	15.5	12.5	15.2	0.75	1	nil
25	Perumal	48/M	25104	55	II	Left diabetic foot-BK Amputation	8	11	15	13	15.5	0.666667	2	nil
26	Perumal	42/M	104962	60	II	PVOD right leg-BK Amputation	10	14	15.8	14	15.8	0.75	2	nil
27	Subburaj	65/M	36141	50	II	Right diabetic foot-BK Amputation	14	18	16.5	14	17	1	2	nil
28	Kaliammal	50/F	13917	45	I	Left diabetic foot-BK Amputation	12	15	15	13	16.2	0.75	2	nil
29	Shanmugam	40/M	45514	50	II	PVOD left foot-BK Amputation	11	14	15	13	16	1	2	nil
30	Arumugam	52/M	15065	60	II	Right diabetic foot-BK Amputation	10	14	14.5	13.5	15.8	1	2	nil

GROUP ROPIVACAINE CLONIDINE PULSE RATE CHART(beats/min)

S.No	GROUP	0 MIN	5 MIN	10 MIN	20 MIN	30 MIN	40 MIN	50 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN
1	RC	90	100	86	85	82	82	80	82	82	82	80	80
2	RC	110	116	102	100	106	104	100	96	96	96	96	94
3	RC	78	84	86	88	82	80	82	84	84	82	80	84
4	RC	84	90	94	94	84	86	86	86	86	84	84	84
5	RC	114	120	120	118	116	116	112	110	110	110	110	110
6	RC	114	124	120	120	120	118	112	112	112	114	112	112
7	RC	82	90	90	90	88	88	86	84	84	82	82	80
8	RC	72	90	88	88	86	88	84	80	84	80	78	78
9	RC	84	98	100	96	86	86	86	84	84	84	84	84
10	RC	78	90	94	76	78	78	78	78	80	80	82	84
11	RC	74	86	82	80	76	72	72	72	72	72	72	70
12	RC	88	100	112	96	90	90	88	88	88	88	90	88
13	RC	80	90	96	96	88	82	82	82	82	80	82	82
14	RC	78	88	90	92	80	80	78	78	78	78	76	76
15	RC	100	110	112	102	102	96	96	96	96	96	94	94
16	RC	78	82	86	80	80	78	78	76	76	76	78	78
17	RC	80	90	94	80	78	78	78	78	76	76	76	76
18	RC	86	90	90	92	88	88	84	82	82	80	78	78
19	RC	78	84	84	84	78	74	74	74	74	76	74	72
20	RC	72	80	80	76	72	70	68	68	68	66	68	68
21	RC	72	72	70	72	72	72	70	68	68	68	68	66
22	RC	76	80	82	82	74	74	70	68	66	66	66	66
23	RC	78	82	88	88	84	80	80	78	78	76	72	72
24	RC	72	70	68	68	66	66	66	64	66	66	64	66
25	RC	80	84	86	86	86	82	80	78	78	78	78	78
26	RC	79	82	82	86	78	74	72	70	72	72	72	70
27	RC	69	74	68	66	68	66	62	64	64	62	62	62
28	RC	93	92	94	92	90	88	86	86	86	86	86	84
29	RC	87	96	100	98	94	92	92	90	90	90	84	82
30	RC	70	80	76	74	72	72	70	70	68	68	70	70

GROUP ROPIVACAINE CLONIDINE SYSTOLIC BLOOD PRESSURE(mmhg)

S.No	GROUP	0 MIN	5 MIN	10 MIN	20 MIN	30 MIN	40 MIN	50 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN
1	RC	130	13	128	128	126	126	128	128	126	126	126	126
2	RC	120	130	126	118	116	116	114	116	116	118	118	118
3	RC	120	120	118	116	120	120	120	120	120	120	120	120
4	RC	126	130	130	130	128	128	128	128	128	128	128	128
5	RC	130	134	140	130	130	130	130	130	130	132	132	132
6	RC	140	140	140	138	138	140	140	140	140	140	140	140
7	RC	110	120	110	110	100	110	106	110	114	116	118	120
8	RC	120	120	120	118	120	120	120	120	120	1220	110	110
9	RC	110	120	120	120	110	110	110	110	110	110	110	110
10	RC	130	136	140	138	130	130	130	130	130	130	130	130
11	RC	120	120	130	118	120	120	120	120	122	120	120	124
12	RC	130	140	134	130	130	130	130	130	130	130	130	130
13	RC	120	130	128	128	124	120	120	120	120	120	120	120
14	RC	130	138	138	138	130	130	130	130	130	130	130	130
15	RC	140	144	146	140	140	140	140	138	138	138	138	138
16	RC	110	118	118	118	120	110	110	110	110	110	110	110
17	RC	140	146	140	140	140	140	140	140	140	140	140	140
18	RC	130	132	132	130	130	130	130	130	130	130	130	130
19	RC	130	134	134	130	130	130	130	130	130	130	130	130
20	RC	140	140	140	140	140	138	138	140	140	140	140	140
21	RC	120	120	120	120	120	120	120	120	120	120	120	120
22	RC	120	124	124	118	118	116	118	120	120	120	120	120
23	RC	110	120	120	120	110	110	110	110	110	110	110	110
24	RC	130	134	134	130	128	128	128	128	128	128	130	130
25	RC	120	120	120	118	118	118	116	116	116	116	120	120
26	RC	120	124	122	120	120	120	120	118	118	118	120	120
27	RC	120	120	120	120	118	118	116	116	116	118	118	118
28	RC	140	140	140	140	140	140	140	138	138	138	140	140
29	RC	140	140	138	138	138	138	138	140	140	140	140	140
30	RC	120	110	120	120	120	120	120	120	120	120	120	120

GROUP ROPIVACAINE CLONIDINE DIASTOLIC BLOOD PRESSURE(mmhg)

S.No	GROUP	0 MIN	5MIN	10 MIN	20 MIN	30MIN	40 MIN	50 MIN	60 MIN	120 MIN	180 MIN	240 MIN	300 MIN
1	RC	80	80	80	78	78	78	78	78	80	80	80	80
2	RC	80	84	84	80	80	76	76	76	76	76	76	76
3	RC	70	70	70	70	66	66	66	66	68	68	68	68
4	RC	78	80	78	78	78	78	76	70	70	70	70	70
5	RC	80	82	82	80	80	80	80	80	80	80	80	80
6	RC	80	80	80	80	78	78	78	78	78	78	78	78
7	RC	70	70	72	72	70	70	70	70	70	70	70	70
8	RC	70	70	68	68	68	68	68	70	70	68	70	70
9	RC	80	80	78	78	78	80	80	80	80	80	80	80
10	RC	80	80	80	80	78	78	76	74	74	74	72	74
11	RC	70	70	74	74	70	70	70	70	70	70	70	70
12	RC	80	80	80	80	80	78	80	80	80	78	78	78
13	RC	80	80	80	80	78	76	78	80	80	78	78	78
14	RC	70	70	70	70	68	68	68	68	66	64	66	66
15	RC	70	70	70	70	70	68	68	68	68	66	66	66
16	RC	70	70	70	70	70	70	70	68	70	70	70	70
17	RC	80	82	82	80	80	80	80	80	80	80	80	80
18	RC	80	80	80	80	78	78	80	80	80	78	80	80
19	RC	80	80	80	80	78	76	76	76	76	74	74	74
20	RC	70	70	70	68	70	70	70	70	68	68	66	66
21	RC	80	80	80	80	78	80	80	78	78	76	76	76
22	RC	80	82	82	80	80	78	78	78	76	76	76	76
23	RC	70	70	70	70	68	68	68	68	68	66	66	66
24	RC	70	70	70	70	70	68	70	70	70	70	70	70
25	RC	80	80	80	80	80	80	80	80	80	80	78	78
26	RC	70	70	72	70	70	68	68	68	66	66	66	64
27	RC	70	70	70	70	70	70	70	68	68	68	68	68
28	RC	70	72	70	70	70	70	72	70	68	68	68	68
29	RC	80	80	80	80	78	78	78	78	78	78	78	76
30	RC	80	80	80	78	78	78	78	76	76	76	76	76

CLONIDINE AS AN ADJUVANT TO ROPIVACAINE IN SCIATIC FEMORAL BLOCK FOR LOWER LIMB SURGERY

ABSTRACT

Background

This is a prospective randomized double blinded study of evaluation of clonidine as an adjuvant to ropivacaine in sciatic femoral block for lower limb surgery **.**

Methods

60 Patients of ASA grade I or II undergoing upper limb surgeries were randomly assigned into two groups, groups R and RC. Surgery was done under sciatic femoral nerve block through Labats approach after confirmation with nerve stimulator. The patients in group R received 30 ml at 0.75% Ropivacaine and 0.4 ml Normal saline. In group RC received 30ml at 0.75% Ropivacaine and 60 micrograms clonidine. In this 30ml mixture, 18 ml given in sciatic nerve block and 12 ml given in femoral nerve block. Parameters observed were time of onset of sensory and motor block, duration of sensory and motor blockade, duration of post operative analgesia, sedation score and side effects.

Observations

There is no significant difference in the onset of sensory and motor blockade in ropivacaine-clonidine group when compared to ropivacaine group. The addition of clonidine to ropivacaine increases the duration of sensory blockade by 184 minutes, duration of motor blockade by 157 minutes and the duration of post operative analgesia by 192 minutes when compared to ropivacaine alone ($P<0.05$). In this study, no significant difference was observed with respect to the pulse rate, systolic and diastolic blood pressure, sedation and saturation.

Conclusion

The addition of clonidine to ropivacaine in sciatic femoral nerve block shows no difference in the onset of sensory and motor blockade but prolongs the duration of both sensory and motor blockade and post operative analgesia, when compared to ropivacaine alone.

Key words

Sciatic femoral nerve block, clonidine, ropivacaine, nerve stimulator.